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BULLETIN OF
THE NEW YORK ACADEMY
OF MEDICINE

MARCH 1944

PRESIDENTIAL ADDRESS*

ARTHUR FREEBORN CHACE

President, The New York Academy of Medicine

THE ACADEMY IN THE VANGUARD

ONE year ago tonight, in assuming the office of President, I spoke to you on the theme, *The Academy Meets The Challenge Of The Future.* This evening I come to you to give an account of our stewardship.

The challenge of the future, I said a year ago, was evident to everyone. Wanting was the knowledge of how best to meet it. In that connection I promised that the Academy would "institute in the immediate future . . . careful and thorough-going studies of the trends and the indicated future developments in medicine and in communal and public health" and furthermore that the Academy would "scrutinize carefully the proposals and plans for the post-war world that are formulated by responsible and authoritative agencies in order that we may be fully informed and in a position to contribute effectively such services as we may be ultimately called on to render."

This promise, I am happy to inform you, has been fulfilled.

Early in 1943, there was formed, under the able leadership of Dr. Malcolm Goodridge, a Committee on Medicine and the Changing Order. Fourteen Fellows of The New York Academy of Medicine, eminent

* Read at the Annual Meeting of The New York Academy of Medicine, January 6, 1944.

for their knowledge and service in the social and economic fields of medicine, were chosen to serve on this Committee. To these were later added thirty-one committee members representing the leaders of thought in the fields of labor, law, social work, nursing, medical education, dentistry and public health.

The Committee is pursuing its work with unremitting energy and devotion. It meets weekly, bringing to its meetings eminent scholars and experts who, in an informal way, present to the Committee their particular knowledges and opinions in a variety of fields related to medicine. The presentations of the speakers are freely discussed by the members, the Committee seeking, in this way, to acquire a broad view of the social, educational and scientific factors that enter into the problems with which it is concerned.

It is the object of the Committee to obtain broad, historical perspectives so that we at the Academy may better envisage the form of society into which the world is being rapidly projected and be the better able to help adapt medicine, in all of its many phases, to the new world pattern.

Our first year of study has convinced us that the social pattern of the immediate future will be influenced by planning on the part of the government, industry, labor and consumers and that the Academy can and must play an active part in the adjustment of medicine and public health to this new social order.

In the development of its work, the Committee has undertaken the preparation and publication of a series of monograph studies devoted to the major individual problems affecting the structure and functions of the medical profession. Now in the process of preparation are monographs dealing with American Medical Practice; The American Hospital; Medical Research; Industrial Medicine; Labor Medicine; The Various Types of Insurances for Medical Services; and Preventive Medicine. Additional monograph studies are planned to deal with Medical Education; Rural Medicine; The History of the Development of the Specialist and its Relations to Group Practice; The Development of the Community, State and National Medical Services; Dentistry; Nursing; Convalescent Care; Psychosomatic Medicine, and Medical Social Service.

The Committee expects that the materials provided by these monographs, together with the subject matter gleaned from its weekly conferences, which are to be continued through 1944, will provide it with

the substance of its final report.

An Editorial Committee, consisting of Dr. Iago Galdston, Mr. Lawrence Frank and Professor Bernhard J. Stern, has begun to prepare the outline of the Committee's Final Report. This report we hope to have finished during 1944, and it is our expectation that it will offer fundamental data and concrete help toward the solution of the problems in medical service which we in medicine must thoughtfully and courageously face.

We are satisfied that our Committee on Medicine and the Changing Order has made good progress during this, the first year of its existence.

Despite our earnest concern with the future, we have not neglected the present and we have met, to the best of our abilities, the added and emergency demands which the war has placed upon us. We have yielded no ground, despite losses in budgetary resources, in fellowship and in personnel. Our Stated Meetings, our Friday Afternoon Lectures, our Annual Graduate Fortnight, our Laity Lectures, in a word, all our educational services to the profession, as well as to the public, have been carried on without remission. In addition, we have had the opportunity to render a number of new services.

The war, as you know, has placed a heavy burden upon our transportation system. Because of that, and at the request of the government, most national scientific organizations have suspended their annual conferences. Yet it is vitally necessary that the workers in science should meet in common periodically, to exchange in person, their views and experiences. Such cross fertilization of the intellect assures the best yield in the fields of science. Since, then, national meetings are impossible, a number of regional meetings could serve the same ends. For this purpose our Committee on Medical Education arranged, in May, 1943, a Conference on Clinical Research.

This conference brought together the research workers of Metropolitan New York for a review and discussion in common of their work and problems in a variety of fields, particularly in medicine, surgery, obstetrics and gynecology. This conference was conducted simultaneously in three separate halls, included twenty-seven presentations and was attended by 500 participants. In this way our Committee on Medical Education helped to overcome the handicaps suffered by the research workers in the war time cancellations of the customary meetings of scientific organizations.

Nor has our Committee on Medical Education remained unmindful of the Challenge of the Future, particularly as it involves medical education. The accelerated medical course which is now being given to thousands of medical students, the curtailment to nine months duration of hospital internships, the restrictions placed upon residencies and other forms of postgraduate instruction and training, dictated by the demands of the war, threaten to unloose upon the public, once peace is established, a host of inadequately trained physicians. No one, may I add, is more acutely aware, and more anxious about the inadequacy of their education and training than the young medical men affected. To this grave problem our Committee on Medical Education is giving most earnest thought and study. It is formulating plans for postgraduate education of the war time graduates in medicine, as well as for the thousands of other physicians who will have been out of civil practice for a number of years.

The Committee on Medical Education furthermore fully realizes the extraordinary opportunity and the momentous responsibility, which now confront medical education in New York City. Devastation, yes, even annihilation has overtaken the chief European centers of medical education. Years, perhaps decades must elapse before these centers can be restored or reëstablished. In the present and immediate future the medical men of all the world, and particularly the twenty-one republics of Central and South America and West Indies, must turn to America, and to a great extent, to New York City for leadership in the medical sciences.

The Committee on Medical Education realizes the pressing actualities of these demands and has given much thought to an appraisal of our resources to meet these needs. New York has, beside the Academy, five great County Medical Societies, five medical schools, and more than two hundred modern hospitals, numerous excellent clinics, and many distinguished teachers and practitioners in the medical sciences. The problem of organizing and utilizing our splendid resources is indeed made more difficult by their very multiplicity. If we are successfully to employ all available means for postgraduate medical education, we need leadership, organization, and coöperation.

This problem is rendered the more perplexing by two additional factors; the one is the certainty that post-war demobilization of our military and naval forces will multiply a hundred-fold the demand for shorter

refresher courses for our own demilitarized doctors; the other is the uncertainty arising from proposed basic changes in our laws governing social economy and medical practice.

The Committee on Medical Education is now searching for an adequate solution: Will the present universities and other teaching institutions be able to expand sufficiently to meet these great demands? Will it be necessary to establish a new and independent school for postgraduate medical education? Or will it be possible for the Academy, working with the medical schools, the County Medical Societies and the great teaching hospitals, to develop an adequate, coöperative organization which will effectively employ our unsurpassed resources for medical education?

A solution is not easily found, yet the Committee feels that central leadership, and complete, unselfish coöperation of all parties will yet provide one.

Of the many other services rendered by the Academy, I can highlight only a few. The Public Health Relations Committee, at the request of the Mayor, has completed an extensive study on the effects of marihuana. The Committee also is working on a study of adolescent boys and juvenile delinquency.

For many weeks the Committee has been studying the details of the organization of the War Industries Training Program and has developed standards for physical fitness for trainees, both men and women, in the various war industries. This has been made the basis for the procedure which is being carried on by the Department of Education in coöperation with the federal authorities.

Early in the year, the Committee issued a report on oleomargarine which helped considerably in removing certain administrative and legislative obstacles in the way of oleomargarine production and has helped to make it a requirement that each pound of oleomargarine contain at least 9,000 units of vitamin A.

The Committee has been helpful in bringing about a meeting of minds in the establishing, formulating and developing of a program for the training of practical nurses. This has helped to obtain the necessary agreements in the field and a budget for the development of this important accessory group of nurses.

In response to a request from a member of the State Grievance Committee, a great deal of time has been given to the study of the present

law concerning abortions and suggestions have been made for legislative change which would close the various technical loopholes that have been made use of by those who perform criminal abortions.

Turning now to still other of the Academy's accomplishments during the past year, we can cite with satisfaction, the aid rendered to the U. S. Public Health Service. The Academy's facilities were placed at the disposal of the United States Public Health Service for a period of six days, during which twelve lectures were given on Occupational Dermatoses. These lectures were largely attended by members of the medical profession in the Army and Navy, particularly those connected with the government manned ordnance plants.

Office space in the Academy was allotted to the Bureau of Procurement and Assignment.

The Fourth Annual Health Education Conference of the Academy was this year devoted to radio. It was attended by one hundred and seventy participants, representing over ninety separate organizations, including representatives of six of the largest broadcasting systems. The problem approached was that of a more effective collaboration with radio in the education of the public in preventive medicine.

The lectures before the Stated Meetings on penicillin, the sulfonamide derivatives and the Lectures to the Laity on "The Methods Of Combating Tropical Diseases Arising From The War," were outstanding.

The election of fifty-two corresponding Fellows in Latin American countries in 1942 resulted in the creation of much good will. The Committee on Medical Education is now also preparing a list of outstanding medical men in the Soviet Union for Fellowship in the Academy.

The establishment of the Florence Ellsworth Wilson Memorial Fund will give us an income of invaluable assistance in obtaining outstanding speakers for the Graduate Fortnight.

The intensified interest of the public in health matters has been a tax upon the personnel and the physical capacity of the Library. The most urgent need of the Academy is for funds which will enable us to meet these demands on our Library, which stands alone, due to the war's devastating effect on so many of the great medical libraries of the world. We must not only be guardians of the intellectual treasures of the past, but we must have available to all who seek knowledge after the war, the most complete records of the medical advances of this period.

The activities of the Academy have actually increased in spite of rigid economies necessitated by the marked increase in operating costs. Our deficit for 1943 was approximately twelve thousand dollars. This represents almost the exact amount lost through admission fees and the cancelled dues of the 322 Fellows now in military service. In this connection I am happy to report that one of our prominent Fellows has again come to our aid with a contribution that effaced our deficit. But I am obliged to advise you that the budget for 1944 does not permit of overdue salary adjustments nor does it allow adequate funds for the purchase of medical books or periodicals for the Library.

The Steering Committee has done and is doing an outstanding work in endeavoring to provide funds that the Academy may continue its invaluable activities and attain its objectives.

These, then, are our achievements: We have clearly formulated our objectives. We are earnestly seeking to anticipate the form of society in which we shall live. We are in the process of adjusting medicine, in its broadest sense, to the new social order. In addition, we have carried on the regular activities of the Academy at a high level and we are meeting those problems arising from the war.

We feel that the year 1944 offers the Academy the greatest opportunities for service in its long and distinguished history, and we are determined that its magnificent work shall never falter, but go on to greater fulfillment—for—

"Time is our Slave and Fortunes.
We need not years for fruition,
Here in our hands behold the key,
Which unlocks the world."

THE TREATMENT OF LOBAR PNEUMONIA AND PNEUMOCOCCAL EMPYEMA WITH PENICILLIN*

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THE therapeutic value of penicillin for patients was first described in the treatment of cases of staphylococcal infection.[1] Even though penicillin has not been found in tests in the laboratory to be as potent in antibacterial action against staphylococci as against pneumococci or hemolytic streptococci, it is, nevertheless, more effective against staphylococci than are the sulfonamide drugs. Consequently, the fact that clinical trials were first attempted in cases of severe staphylococcal sepsis constituted a rational procedure and subsequent experience has yielded highly satisfactory results in this type of infection that has not been uniformly amenable to sulfonamide therapy.[1,2,3]

In accord with experimental studies which have demonstrated the antagonistic action of penicillin against a wide variety of pathogenic bacterial species, estimates of the value of penicillin therapy have been broadened beyond cases of staphylococcal etiology to include many different kinds of infection in man. The most recent results have been recorded and summarized in the comprehensive report of Keefer, Blake, Marshall, Lockwood, and Wood.[3]

The present report is limited to a description of the results obtained in the treatment of pneumococcal pneumonia and pneumococcal empyema with penicillin.

The unusually high degree of antibacterial activity of penicillin, *in vitro*, against pneumococci was demonstrated in the original report of Fleming[4] and has been repeatedly observed by others.[5,6,7] *In vivo*, the curative action of penicillin in mice has been demonstrated against many

* The investigation of empyema was aided through the Commission on Pneumonia, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Division, Office of The Surgeon General, United States Army.
Read November 4, 1943 before the Stated Meeting of The New York Academy of Medicine.

hundred thousand lethal doses of highly virulent strains of different serological types of pneumococci.[8,9] Although some variation in the sensitivity of strains has been suggested, pneumococci appear to be one of the pathogenic bacterial species most vulnerable to the action of penicillin.

When the experimental results just mentioned are taken into account in connection with the proven low toxicity of penicillin for man, the favorable outcome of the treatment of pneumococcal infections with penicillin becomes a reasonable expectancy.

Forty-six cases of pneumococcal pneumonia and 8 cases of pneumococcal empyema comprise the present series. In view of the fact that the methods of treatment and the details of the study of the cases of pneumonia and of the cases of empyema were different, each of the subjects is presented separately.

I. The Treatment of Pneumococcal Pneumonia with Penicillin

Although the number (46) cases of pneumonia is not great, the selection of patients to be treated with penicillin was limited to those who, on admission, exhibited lobar consolidation and a degree of severity indicating the probable pneumococcal etiology of the infection. Even though therapy was at times instituted before the bacteriology was reported there were only three instances in which the specific etiology was undetermined. The data in Table I on the distribution of serological types of pneumococci responsible for the infections and also the incidence of bacteriemia indicate that the cases used for treatment consisted of a representative sample of pneumococcal pneumonia with respect to kind and severity.

In the patients with pneumonia the observations have been directed not only toward determining the value of penicillin as an effective curative agent but the attempt has also been made to estimate the range of dosage that was sufficient without constantly employing amounts that might be excessive and, therefore, unnecessary. For this latter purpose the number of injections and the duration of treatment were arbitrarily altered in order to observe the response to limited treatment.

Material and Route of Administration. The penicillin was supplied in a dry powder contained in sealed ampoules. It was kept constantly in the ice box. Solutions for injection when prepared in advance were also kept in refrigeration but were not retained for longer than a day

or two. It may be noted in passing that solutions used in the laboratory for experimental purposes have been found to retain potency for several weeks.

Penicillin in solution was given to patients by repeated injections either intravenously or intramuscularly. For intravenous injection the powder was dissolved in physiological salt solution or sterile water in the ratio of 1000 units to 1-1.5 cc. of solution. For intramuscular injection the ratio was 1000 units to 0.3 cc. of solution so that the usual individual dose of 10,000 units was contained in a total volume of 3.0 cc.

Some of the patients were treated solely by intravenous injections, others only by intramuscular injections, and still others received intravenous medication for the first few doses followed by intramuscular injections for subsequent treatments. The intramuscular route proved to be effective and was, for convenience sake, frequently employed. However, in cases which appeared seriously ill on admission, one to four injections were given intravenously and when improvement seemed evident subsequent injections were given intramuscularly.

Dosage of Penicillin and Spacing of Treatment. The amount of penicillin per dose ranged from 10,000 to 25,000 units, most frequently the former. The repeated doses which were given in series were made at three hour intervals.

Several procedures were employed which differed in the following respects:

1. Number of repeated injections at three hourly intervals which comprised one series of treatments. The single series varied from three to eight injections, the latter lasting for twenty-four hours.

2. The lapses between each series of injections which were given from day to day were not always kept constant. Charts are presented which illustrate the clinical courses of patients who received interrupted treatment.

3. The number of consecutive days of treatment varied from one to four. The information which emerged from altering the duration of treatment will be subsequently discussed.

Etiological Pneumococcal Types. From Table I it may be noted that in 32 (69 per cent) of the cases the infecting pneumococci belonged to serological Types I–VIII. Fourteen patients had bacteriemia (30 per cent). Among the cases in which the pneumonia was due to pneumococci, Types I–VIII, 13 (40 per cent) has bacteriemia.

TABLE I

SUMMARY OF CASES OF PNEUMONIA TREATED WITH PENICILLIN

Pneumo Types	*No. of Cases*	*Blood Culture* +	—	*Duration of Treatment Days* 1	2	3	4	*Total Dosage of Penicillin (Range) Oxford Units*	*Response* Definite	Indefinite	Died
I	11	4	7		2	5	3	60,000-250,000 Av: 148,000	10		1
II	6	3	3		1	3	2	70,000-170,000 Av: 113,000	6		
III	1	1	0				1	140,000	1		
IV	1	1	0			1		110,000	1		
V	5	1	4		1	2	2	70,000-190,000 Av. 115,000	4	1	
VII	2	1	1		1		1	70,000-140,000 Av: 105,000	2		
VIII	4	2	2	1		2	1	70,000-120,000 Av. 90,000	3		1
IX	1	0	1			1		120,000			1
XI	2	0	2	1			1	40,000-130,000 Av: 85,000	2		
XII	1	0	1			1		90,000	1		
XV	1	0	1			1		120,000	1		
XIX	1	0	1			1		90,000	1		
XX	1	1	0		1			50,000	1		
XXIX	1	0	1			1		95,000		1	
Unclass.	7	0	7	2	1	3	1	30,000-160,000 Av: 100,000	5	2	
TOTAL	45	14	31	4	7	21	12	30,000-250,000 Av. 105,000	38	4	3

Outcome of Treatment. Among the 46 patients treated with penicillin, three died. (Mortality 6.5 per cent). Of the patients who died, one was a 69 year old man who had severe congestive heart failure together with pneumonia and bacteriemia due to pneumococcus, Type VIII. His blood culture, taken on the second hospital day, was sterile and his temperature was below 100°F. but the heart failure was worse. He died 36 hours after admission. The second fatal case had pneumonia and bacteriemia, pneumococcus, Type I, superimposed on some chronic pulmonary disease. His blood culture of the second hospital day was sterile but there was no clinical improvement. Subsequent therapy included sulfadiazine and antipneumococcus serum, Type I, but it was ineffectual. The third fatal case had pneumonia due to pneumococcus, Type I, but no bacteriemia. He did not appear severely ill but did not respond to penicillin. He died on the third hospital day a few hours after pulmonary edema developed.

Of the 43 patients who recovered, in four instances therapy was not followed by rapid clinical recovery. The result is, therefore, listed as indefinite, although the final diagnosis in one patient was primary atypical pneumonia and the other three had prolonged courses, in one of whom there was delayed resolution which was unexplained; in another, who after several weeks developed pneumothorax, tuberculosis was suspected; and the third patient had bronchiectasis on which the pneumonia was superimposed. Even though these three latter cases are classed as ineffectively treated, the sterilization of the bacteriemia by penicillin in two of them will be subsequently mentioned.

The remaining 39 patients (84 per cent) recovered in a manner that indicated the high degree of effectiveness of penicillin.

The rapidity in the drop in temperature was striking, the change occurring usually within the first 12 to 20 hours, and the impression was that the response occurred somewhat more quickly than that observed after sulfonamide therapy. The alleviation of symptoms was marked. The respirations were slowed to normal rates coincident with improvement although cough persisted for several days. There were no untoward depressive physiological reactions referable to the rapid critical change in the condition of the patients. Although no data have been collected with regard to the rate with which clearing of the consolidated area occurred, the impression has been formed that resolution progressed more rapidly than that observed following sulfonamide therapy.

The leukocyte count was unaffected by penicillin and returned to normal within four to six days.

No toxic reactions were observed, except an occasional pyrogenic reaction which came on about one hour after an injection and lasted approximately two hours. The degree of soreness at the site of intramuscular injection was never severe, nor was there any swelling or redness or appreciable local irritation.

The hematopoietic system exhibited no signs of irritation. No special changes in urine were noted. No psychic or neurological abnormalities were evident.

Duration of Treatment. From an analysis of the data given in Table I under the heading "Duration of Treatment, Days," information is available concerning the length of time that therapy may be required. In all of the patients without complications an initial definite response was noted within 16 to 20 hours of beginning treatment as evidenced by sharp drop in temperature and symptomatic improvement. The subsequent course varied, however, depending on the length of time treatment was continued.

From Table I it may be seen that most of the patients, 31, were treated for 3 to 4 days. Among this group, when no complicating factors existed, the initial improvement persisted as permanent cure.

The complications which delayed prompt and complete recovery were empyema and chronic pulmonary disease on which pneumonic consolidation was superimposed. Among the cases with complications other than empyema it may be stated that when treatment was switched to sulfadiazine no appreciable response was obtained.

Clinical Response in Relation To Dosage. In attempting to estimate the amount of penicillin necessary to suppress the infection, the injections in selected patients were arbitrarily interrupted after the first or second day of treatment. Most of the patients in these groups received 30,000 to 40,000 units per day in divided doses of 10,000 units each. The reaction of the infection to the measured treatment has served as a source of information with regard to the degree and duration of the response in relation to quantity of the drug.

Table II contains data derived from patients in whom injections of penicillin were arbitrarily withheld following either one or two days of therapy. An analysis of the material in Table II reveals the following:

In each of the seven cases in which penicillin therapy was adminis-

TABLE II

COURSE OF PATIENTS IN WHOM ADMINISTRATION OF PENICILLIN WAS INTERRUPTED AFTER ONE OR TWO DAYS OF THERAPY

Patient	*Admin. Day of Disease*	*Pneumonia Type*	*Blood Culture*	*Penicillin—1st Day*		*Penicillin—2nd Day*		*Initial Response*	*Subsequent Course*
				No. of Injections	*Daily Amount*	*No. of Injections*	*Daily Amount*		
J. Z.	3rd	Unclassified	—	3	30,000	—	—	Yes	Rapid Recovery
M. H.	3rd	VII	—	3	30,000	—	—	Yes	Relapse
D. R.	2nd	Unclassified	—	4	40,000	—	—	Yes	Rapid Recovery
V. J.	2nd	XI	—	4	40,000	—	—	Yes	Rapid Recovery
B. M.	3rd	II	—	4	40,000	—	—	Yes	Relapse
F. T.	?	XX	+	5	50,000	—	—	?	Prolonged
J. G.	3rd	VIII	—	7	70,000	—	—	?	Died
L. T.	4th	II	—	4	40,000	3	30,000	Yes	Rapid Recovery
A. K.	3rd	V	—	6	60,000	3	30,000	Yes	Relapse?
J. B.	5th	II	—	4	40,000	4	40,000	Yes	Relapse?
A. L.	3rd	Unclassified	—	4	40,000	3	30,000	Yes	Relapse
E. F.	1st	II	+	4	40,000	5	50,000	Yes	Relapse
M. B.	4th	V	+	4	40,000	5	25,000	Yes	Empyema
O. B.	?	I	+	3	30,000	3	30,000	?	Died

tered on the first day and then interrupted, there was a significant drop in temperature to below 101° in 16 to 24 hours but permanent cure was not uniformly effected.

In each of the two patients in the one day group with bacteriemia a second blood culture taken on the second hospital day was sterile.

With the exception of the patient who died 36 hours after admission, symptomatic improvement accompanied the early fall in temperature.

Complete cure followed a single series of injections given for one day in three cases. However, it should be noted that the pneumococci isolated from their sputum belonged to serological types not usually associated with severe pneumonia. Consequently, the mildness of the pneumonia may have promoted the striking response even though the patients were treated early in the disease, i.e., 3rd, 2nd and 2nd days respectively.

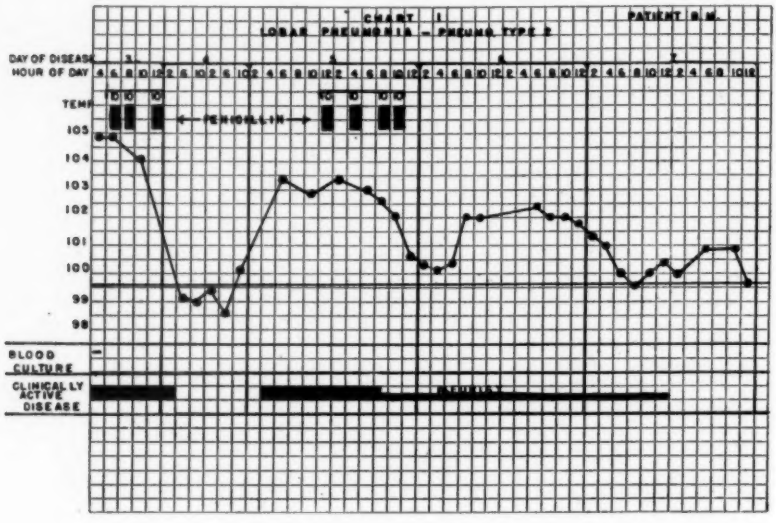
In the three remaining cases who recovered and in whom treatment was withheld after the first day, a relapse of the infection occurred. Recovery, however, promptly followed the reinstitution of treatment.

In the patients who were treated on *two consecutive days* before withholding therapy, with the exception of the fatal case, improvement followed the first day of therapy. Consequently, the second series of injections was given after improvement had begun. In each instance of bacteriemia in this group, the blood culture taken on the second day was sterile and remained so.

As to the final outcome following two days of treatment one of the patients made a rapid and permanent recovery, whereas, among the remaining cases in this group, two had transient rises of fever to 101° to 102° appearing 48 hours after the last injection and spontaneously receding within two days, and the other two had definite relapses.

From a consideration of the findings given in Table II it appears that penicillin in the dosages employed evoked rapid early improvement indicating the high degree of sensitivity of the infecting pneumococci to penicillin. It is also evident that relapse was liable to occur if treatment was not extended longer than two days.

From the standpoint of chemotherapy the importance of the development of type specific immunity in promoting permanent recovery from pneumococcus infections has been illustrated both experimentally and clinically in relation to sulfonamide therapy. MacLeod[10] demon-

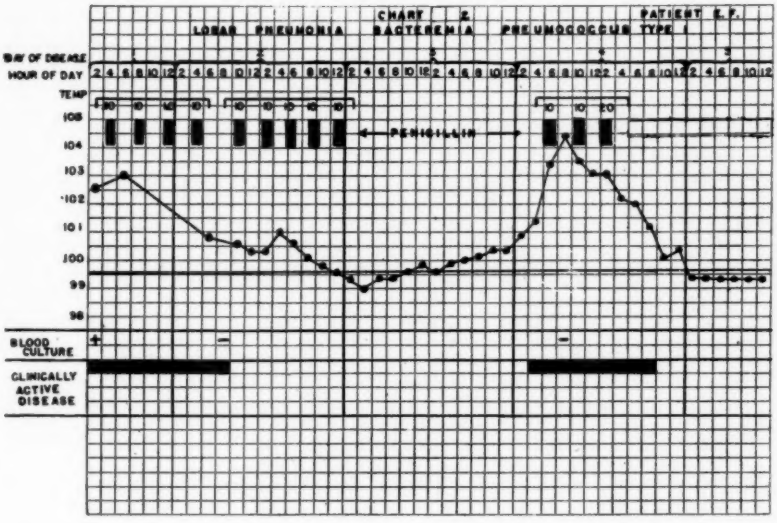


strated in mice that the suppression of pneumococcal infection by sulfapyridine was made permanent by the appearance of type specific immunity. In pneumonia the observation has been repeatedly made that patients treated early (first to third day) with appropriate sulfonamides are liable to relapse if treatment is stopped in one or two days.

In comparing the experience with sulfonamides with that encountered with penicillin it seems probable that the continuance of treatment as determined by the day of disease is of equal importance with either of the drugs.

For purposes of demonstrating graphically the quantitative relationships between dosage and its effect on the infection with particular reference to the duration of the remission after premature withdrawal of treatment, the details of the courses of two patients are given in Charts 1 and 2.

Chart 1 is that of a patient with pneumonia due to pneumococcus, Type II, who was admitted on the 3rd day of disease. Following the details of the temperature chart it may be seen that the last dose of penicillin on the first day was given at approximately 12 midnight and that the temperature became normal between 2 and 6 the following morning—12 hours after beginning therapy. That the therapeutic effect



was not solely antipyretic is evidenced by the marked alleviation of symptoms during the afebrile period. The patient became worse at about 4 o'clock on the morning of the 3rd hospital day, approximately 28 hours after the last injection. In view of the fact that measurable amounts of penicillin have been found by Rammelkamp and Keefer[11] to disappear from the blood within 3 hours after injection, the disease in this patient was restrained for approximately 25 hours after the blood level of penicillin was presumably zero.

The second series of injections of penicillin given on the 3rd hospital day was also followed by a definite response. A dry pleurisy persisted for two additional days but complete recovery was not further delayed.

Chart 2 is that of a patient whose course was particularly instructive. He was admitted eight hours after a chill which initiated the attack of pneumonia. Injections of penicillin were begun promptly. His blood culture was positive for pneumococcus, Type 1. His course illustrates the importance of taking into account the day of disease on which therapy is begun in determining the duration of therapy. In this patient two series of injections on two consecutive days were given before withdrawal of treatment. His response to the first four injections of the first

day occurred, as indicated in Chart 2, within 16 hours. A second blood culture taken five hours after the last previous injection of penicillin was sterile. The initial early improvement was maintained for approximately 28 hours after treatment was stopped. A relapse then occurred abruptly, although a blood culture taken at the height of the febrile exacerbation was negative.

Penicillin therapy was again instituted on the fourth day. Subsequently in this case sulfadiazine was given as supplementary treatment during the latter part of the fourth day because the patient was encountered early in the trials of penicillin before its efficiency for pneumonia had been well established. Permanent recovery occurred on the 6th hospital day.

The course of the two patients just described, in addition to illustrating the rate of response, also demonstrates the duration of the period of remission after premature interruption of treatment.

Results comparable to those just described have been observed in other patients who were followed in a similar manner. In summary, they indicate that, in the average uncomplicated case of pneumonia, the administration of 30,000 to 40,000 units per day in divided doses initiates improvement. Furthermore, the remission evoked by the therapy endured for approximately 20 to 28 hours before the effect of the penicillin was lost.

These findings have afforded useful information in formulating a complete course of treatment with respect to quantity and spacing of dosage.

Additional data of a similar character have been derived from an analysis of the course of the patients with bacteriemia in relation to the injections of penicillin which they received.

Effect of Penicillin on Bacteriemia. Fourteen of the patients had bacteriemia on admission. In each instance following penicillin therapy the second blood culture was sterile. In seven of the patients the time relationships between the second blood culture and the last previous dose of penicillin is sufficiently definite to offer information concerning the duration of the sterilizing effect. The findings are contained in Table III.

The quantitative range of dosage during the first 24 hours in this particular group of bacteriemic cases was from 30,000 to 105,000 units. The differences in amounts of penicillin that were administered oc-

TABLE III

AMOUNT OF PENICILLIN EFFECTIVE IN ALTERING BACTERIEMIA*

Pneumo Type (Patient)	*1st Blood Culture*	*Amt. of Penicillin before 2nd Bl. Culture Units*	*Route of Administration*	*2nd** Blood Culture*	*Interval between previous dose of Penicillin and 2nd Blood Culture*
I (J. S.)	+	105,000	75,000 Intravenous 30,000 Intramuscular	—	3 hrs.
I (J. St.)	+	90,000	25,000 Intravenous 65,000 Intramuscular	—	5 hrs.
II (M. L.)	+	60,000	Intravenous	—	6 hrs.
II (E. F.)	+	40,000	Intravenous	—	9 hrs.
III (B. R.)	+	40,000	Intravenous	—	5 hrs.
VIII (J. G.)	+	60,000	Intravenous	—	16 hrs.
I (O. B.)	+	30,000	Intravenous	—	10 hrs.

*In the six other cases which had bacteriemia on admission the 2nd blood culture was sterile, but it was not taken until the 2nd or 3rd day of hospitalization.

**In each instance the 2nd blood culture was taken approximately 20-24 hours after the 1st.

curred for the most part in connection with explorations of dosage which was altered as experience developed. That the blood stream was cleared in each instance is striking evidence of the potency of penicillin in its antipneumococcal action.

It is of further interest to note from Table III the time of the last previous dose of penicillin in relation to the time of taking blood for the second culture. From the figures in the table it may be seen that intervals of from 3 to 16 hours elapsed but that the bacteriemia did not return. By the method which they employed, Rammelkamp and Keefer[11] found that penicillin was detectable in the blood for 30 to 210 minutes after intravenous injection, the time varying according to the dosage of the drug. On the basis of the figures of these authors, it may be estimated that, in the bacteriemic patients described in Table III, the initial clearing of the blood was maintained in different patients for varying periods of time up to at least 13 hours after circulating penicillin was presumably no longer detectable. Consequently, the damaging effect of penicillin on the invasive pneumococci appears to have restrained their regrowth for an appreciable period after the blood level ceased to be measurable.

Each of the patients of Table III received penicillin intravenously. Whether the rapidity and persistence of the clearing of the blood of pneumococci is best accomplished by intravenous medication has not been determined since comparable studies have not been made following intramuscular injections. The findings in the bacteriemic cases when combined with the results illustrated in the previous Tables and Charts suggest that the maintenance of a definite level of penicillin continuously may not be a necessary detail of satisfactory treatment.

Discussion of Factors Involved in the Application of Penicillin to the Treatment of Pneumonia

Duration of Treatment. On the basis of the experience described in this article it seems apparent that in order to avoid relapses, treatment should be extended over three or four days or for longer periods under special conditions. As stated earlier the duration of treatment is influenced by the day of the disease on which it is started since a remission effected early in the infection (first to third day) may not be maintained unless treatment is continued until the elements of immunity or other factors in the evolution of the disease become operative.

With regard to continued repetitions of injections the data have indicated that when an interval of 12 to 16 hours was permitted to elapse between daily treatments the results were as satisfactory as those obtained by maintaining therapy throughout 24 hours. The special studies demonstrate that the arrest of the infection caused by penicillin was continued beyond the period during which penicillin would be expected to be detectable in the circulating blood.

The reports of Florey and associates[1] and of Rammelkamp and Keefer[11] have described the rapid excretion of penicillin in the urine and also the distribution of the drug in normal body fluids following parenteral injection. However, the extent to which penicillin penetrates into inflamed areas, or the concentration or the persistence of the product in an active state in the extravascular sites of the infection within tissues has not been determined. Whether or not alterations in permeability and diffusion which membranes undergo as a result of inflammation affect the dissemination of penicillin has not been determined.

In interpreting the protracted effect by which the abatement of the infection persisted after the disappearance of circulating penicillin, it seems possible that the result may be dependent upon the retention of penicillin at the local site of the infection for a longer period of time than in the circulating blood, or that the damage inflicted by temporary contact between penicillin and pneumococci is sufficiently severe to delay the further multiplication of organisms.

On the basis of the response of patients, therefore, four injections daily at three hour intervals on three to four successive days has proved satisfactory.

Route of Injection. For the cases of relatively moderate severity, the intramuscular route of injection has been found to be efficacious. However, in patients appearing seriously ill or in those with bacteriemia, the results following intravenous therapy as measured by clinical improvement and disappearance of bacteriemia (Table III) indicate the effectiveness of the intravenous route, which may be preferable for the first few injections.

Amounts per Dose. 10,000 units have been the routine amount employed for intramuscular injection. 10,000 or 25,000 units have been given in intravenous injections, depending on the severity of the case.

Suggested Plan of Treatment. Consolidating the findings that have

been discussed above, the following procedure is tentatively outlined.

Cases of Moderate Severity: 10,000 units of penicillin given intramuscularly every three hours for four doses on each of three and possibly four successive days.

Seriously Ill Cases: 25,000 units given intravenously every three hours for the first two doses of the first day, followed by 10,000 units intramuscularly at three hour intervals for the second two doses of the first day. Subsequent treatment of the second, third, and fourth day to follow plan outlined for cases of moderate severity, i.e., four doses of 10,000 units every three hours for each day.

It is obvious that variations in the clinical course of individual cases may require special alterations in treatment. It should also be emphasized that the above suggestions are not presented as established recommendations but that they represent a current appraisal based on the objective data contained in this report. In view of the low toxicity of penicillin, more extensive therapy than that oulined may be employed without the hazards of serious reactions. However, this study has been directed toward an attempt to define quantitatively the relation of clinical response to therapeutic dosage.

Comparative Value of Penicillin and Sulfadiazine in Pneumonia. Our experience indicates that the therapeutic value of penicillin in pneumonia is at least equal to that of sulfadiazine, and, in addition, there are certain well defined conditions that make the use of penicillin particularly advantageous. They may be summarized as follows:

1. The fact that, up to the present time, no significant toxic manifestations have been noted in association with the administration of penicillin is of special interest. A few cases of urticaria have been described[3] (none in the present series) but the evidence is inconclusive that the eruptions were based on the development of sensitivity. It is, furthermore, uncertain whether such reactions were caused by penicillin or by some contaminating ingredient present in the preparations.

2. Penicillin is particularly serviceable when pre-existing sensitivity to the sulfonamide drugs contraindicates their use, or when sulfonamide toxicity develops during treatment before the infection has been completely overcome.

3. Penicillin has been shown experimentally to be highly effective against sulfonamide-fast pneumococci.[9, 12, 13] In the second part of this article which deals with the local use of penicillin in the treatment of

empyema, the value of penicillin in patients suffering from infections caused by sulfonamide-resistant pneumococci will be described.

It is also of interest to record briefly the favorable response to penicillin of two patients with lobar pneumonia and bacteriemia due to pneumococci refractory to sulfadiazine.

One of the patients in the present series was admitted to the hospital on the seventh day of pneumonia after having received sulfadiazine continuously from the beginning of his illness but without improvement. On admission, in addition to lobar consolidation, he also had bacteriemia due to pneumococcus, Type VII, and a blood level of sulfadiazine of 6.6 mgms. per cent which remained from the pre-admission treatment. By laboratory tests the strain derived from the blood culture proved to be sulfonamide-fast.

Under penicillin therapy the blood culture became sterile within 24 hours and the patient recovered uneventfully in spite of the fact that he also had lymphatic leukemia.

A second instance of infection with a sulfonamide-resistant strain of pneumococcus successfully treated with penicillin was that of a 63-year-old female* who had had pneumonia and an intermittent bacteriemia due to pneumococcus, Type VIII, for approximately 4 weeks before penicillin therapy was instituted. Early in her disease she also developed empyema which was treated surgically by rib resection and drained satisfactorily. She had received sulfadiazine continuously for 4 weeks without permanently altering the bacteriemia. She had also received Type VIII antipneumococcus serum with only temporary improvement. There were no definite signs of endocarditis. On the day following the first injection of penicillin her blood became sterile and remained so. The pneumonia subsided.

In laboratory tests the pneumococci from both the blood culture and the empyemal pus were found resistant to sulfadiazine.

4. Although as yet unsubstantiated by objective data, it seems likely that penicillin sterilizes the blood stream in cases of bacteriemia and suppresses the active infection at a more rapid rate than does sulfadiazine. Although in many instances this difference may not be of special significance, nevertheless in cases of unusually severe infection, the speed of effect may be particularly desirable.

* This case was under the care of Dr. Robert C. Schleussner at the Lenox Hill Hospital and is reported with his permission.

Even though the use of penicillin has the definite advantages just mentioned, the extent to which its widespread use in large numbers of cases of pneumonia would markedly alter mortality statistics is not clear. Analyses of causes of death in cases of pneumonia treated with the sulfonamide drugs[14] have brought out the fact that the majority of the fatalities are due to a variety of complicating circumstances that would not in themselves be overcome even by a more potent anti-pneumococcal drug.

II. The Treatment of Pneumococcal Empyema by the Intrapleural Injection of Penicillin

This study of pneumococcal empyema has been directed toward determining the possible usefulness of chemotherapeutic agents introduced locally as a medical method of treatment which might obviate surgical intervention. In spite of the fact that there seems to have been a decrease in the incidence of empyema caused by pneumococci since the introduction of chemotherapy for pneumonia, the administration of the sulfonamide drugs either by mouth or intravenously has not proved satisfactory in the treatment of empyema after the complication has developed.

At the beginning of the present inquiry observations were made on the course of empyema following the intrapleural injection of sulfadiazine. As a curative measure the initial attempts were unsatisfactory since the pneumococci causing the pleural infections were found to retain viability in the presence of large amounts of the drug and the patient's illness remained unchanged. Consequently, penicillin was employed for local injection.

Up to the present time eight patients with pneumococcal empyema have been treated by the introduction of solutions of penicillin into the infected pleural space. The empyemata, with one possible exception, deevloped as a complication of lobar pneumonia.

Although the details of this report deal with the efficacy of penicillin introduced locally into the empyemal cavities, before proceeding with a description of the methods and results, it is of interest to record briefly some of the observations which were made in connection with local sulfonamide therapy.

The findings are illustrated by the course of one of the patients who was first treated with sulfadiazine and later with penicillin injected

intrapleurally (See Chart 3). After the introduction of sulfadiazine into the empyemal cavity of this patient the sulfonamide content of the exudate reached 415 mgms. per cent. However, on examination of the exudate, pneumococci were seen in direct smears and were viable on culture.

In seeking an explanation for the inactivity of the drug against the organisms as exemplified in the case just mentioned, tests were made for the presence of sulfonamide inhibitors in samples of empyemal exudate obtained from this and other patients. Experiments were also carried out to determine the degree of sulfonamide fastness possessed by several strains of pneumococci derived from empyemal pus.

The results may be briefly summarized as follows:

1. Estimation of the presence of sulfonamide inhibiting substances in pneumococcal pus from cases of empyema.

Five different speciments from four different patients were tested. The method described by MacLeod[15] was employed using a strain of B. coli which was cultivated in an inhibitor-free medium in the presence of varying quantities of sulfadiazine. Exudate was then added and its effect on growth observed. The results obtained in each of the tests failed to reveal the inactivation of sulfadiazine by any of the specimens.

2. Tests for sulfonamide-fastness of empyemal strains of pneumococcus.

Six strains from patients with empyema have been tested by *in vivo* methods, which consisted of infecting mice intraperitoneally and treating them with sulfadiazine, *per os*, twice daily for four days. Five of the strains came from the pleural exudate of patients who were treated at the onset of the pneumonia with sulfadiazine. With each of these strains some degree of drug resistance was evident in that an amount of sulfadiazine sufficient to cure mice infected with laboratory strains of pneumococci was incapable of preventing death in mice infected with empyemal strains.

The sixth strain, however, derived from a patient treated from the beginning with penicillin alone had no degree of drug fastness either to sulfadiazine or penicillin.

Although the findings just outlined are too limited to warrant final conclusions, they suggest that, in cases of pneumonia which develop empyema while receiving sulfonamide drugs, the strain derived from

the pleural exudate may exhibit sulfonamide-resistance. On the other hand, if no sulfonamide therapy has been administered, the empyemal strain may be found to be drug susceptible.

That penicillin warranted trial in this type of infection is indicated by the fact that its antibacterial action against pneumococci is equally potent irrespective of the presence or absence of sulfonamide-fast qualities.[9, 12, 13]

In attempting to develop an effective but uncomplicated method by which penicillin may be utilized locally in pneumococcal empyema, the patients receiving treatment have been studied by correlating their clinical course with the results of laboratory examinations of specimens of pleural exudate derived from the treated area.

The findings have been used as an indication of the degree of effectiveness of varying dosages of penicillin and also as a guide in determining the extent to which repeated injections were necessary.

Material and Methods

In pursuing the studies, samples of pleural effusion were obtained by bedside aspiration at frequent intervals and examined for the presence of viable pneumococci. When pus suspected of containing penicillin was cultured, the specimen was first centrifuged and washed with physiological salt solution in order to avoid transferring a portion of the antibacterial agent contained in the exudate to the broth used for culture media. It may be noted, however, that in comparable tests using 0.1 cc. of specially prepared exudate added to 5 cc. of broth, the preliminary washing did not yield results different from that obtained by adding the same amount of pus directly to the culture media. It seems unlikely that the special technique is necessary as a routine procedure in determining the presence or absence of viable organisms.

In some instances, tests for the presence of penicillin in the exudate were made in order to estimate the duration of its activity following instillation. The method most frequently employed consisted of determining the capacity of the supernatant fluid of centrifuged specimens of effusion to protect mice against infection with pneumococci heterologous in type to that derived from the patient. By this procedure, active penicillin was detected in the exudate for as long as 48 hours after injection in four patients and 72 hours in another patient but was not demonstrable in speciments obtained on the 5th or 6th day following

treatment. As will be discussed later, the duration of sterility has served as a supplementary guide in establishing the quantity and frequency of injections that comprised effective therapy.

Concentration of Penicillin in Solution Used for Injection. Solutions were most commonly made up in a concentration of 1000 units of penicillin in 1 to 1.5 cc. of physiological salt solution. The quantity of solution injected was never in excess of the amount of exudate removed. However, since the largest single dose injected intrapleurally was 40,000 units in 50 cc. and since the amount of exudate aspirated was usually more than 50 cc., the necessity of using a more concentrated solution in order to introduce the desired number of units did not frequently occur. In view of the moderate irritating effect of penicillin on the serous surface of the pleura as indicated in Table IV, the concentration may, under some circumstances, require consideration.

Clinical Course and Laboratory Findings of the Patients

The results derived from the study are given in the form of a brief resume of the course of each patient. Charts of four of the patients are included. X-ray photographs, taken before treatment was begun and after recovery, of 6 patients are appended at the end of this article.

Case 1. Patient A.Mc., male, white, age 57 years.

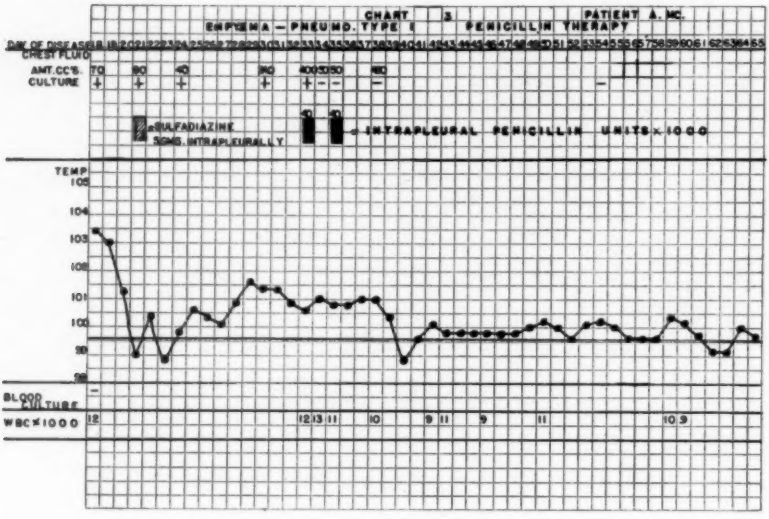
Diagnosis: Lobar pneumonia, bacteriemia, empyema, Pneumococcus, Type I.

The patient was admitted to our wards on the 21st day of illness. In the early stages of pneumonia he had been treated with sulfadiazine. The blood culture became sterile and pneumonia subsided following sulfadiazine therapy but signs of pleural effusion developed. On three separate occasions during the first two weeks of the patient's illness purulent material containing Type I pneumococci was obtained by thoracentesis. One week after the last of the preceding aspirations the patient came under our observation.

The patient's course is illustrated in Chart 3.

From Chart 3 it may be seen that the local treatment of empyema first consisted of 5 gms. of sulfadiazine injected intrapleurally. As mentioned earlier the failure of sulfadiazine to sterilize the cavity was accounted for by the drug-fastness of the infecting strain.

At the time of the first injection of penicillin 400 cc. of thick puru-



lent exudate containing many pneumococci were withdrawn before introducing 40,000 units contained in 50 cc. of isotonic salt solution.

In a sample of exudate obtained on the day following the first treatment, misshapen gram positive forms were seen in direct smears, but cultures were sterile. In a specimen obtained 48 hours after treatment, no gram positive forms were seen; cultures were sterile. At the time of the latter thoracentesis a second dose was administered consisting of 40,000 units. Although two subsequent samples of pleural exudate were obtained 3 and 17 days respectively after the second treatment, pneumococci could not be seen in or cultivated from either specimen.

From a clinical standpoint the patient's general condition was satisfactory throughout the period of treatment although convalescence was somewhat protracted. A low grade fever (100°F) continued for 30 days. During this period discomfort in his chest was present but was not severe. There were some night sweats and a moderate leukocytosis was maintained. However, when the temperature became normal, the evidences of infection disappeared.

Repeated x-ray examinations of the chest reevaled the gradual clearing of a homogenous shadow over the affected area. At a final x-ray examination made two months after discharge from the hospital, the

X-RAY PHOTOGRAPHS OF CASE 1.

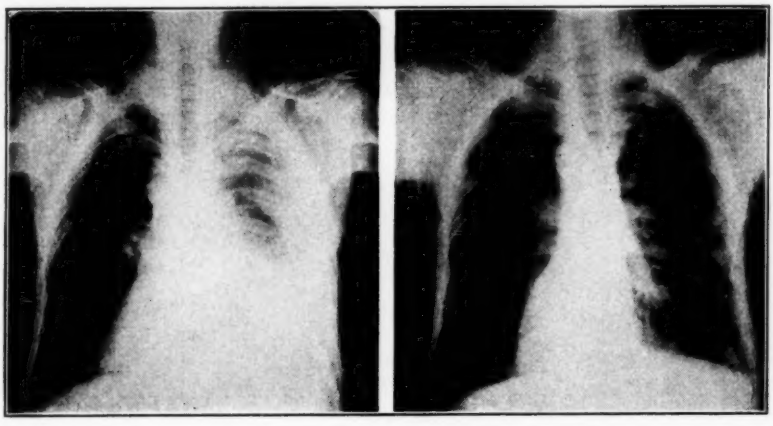


Fig. 1 Before penicillin therapy. Fig. 2 Two months after leaving hospital.

only evidence of abnormality consisted of a small localized band of increased density in the left lateral costophrenic angle.

Resume: Total Number of Intrapleural Injections of Penicillin: Two.

Amount per Dose: 40,000 units.

Total Amount: 80,000 units.

Result: Pleural exudate sterile 24 hours after first treatment. No relapses. Recovery complete with limited residual pleural thickening.

Duration of Hospitalization After Beginning of Treatment: 42 days.

Case 2. Patient E.M., male, colored, age 35 years.

Diagnosis: Lobar pneumonia, bacteriemia, empyema (multiple foci). Pneumococcus, Type VIII.

The patient was treated for the first 10 days with sulfadiazine by mouth. Blood culture became sterile but high fever persisted. Empyema was detected on 6th hospital day. Sulfonamide-fastness of empyemal strain was demonstrated by laboratory tests.

The first intrapleural injection of penicillin (20,000 units) was given on the 10th hospital day. Three additional doses (15,000, 20,000, and 25,000 units respectively) were given into the same site as that of the first injection. The latter treatments were administered on the 2nd,

X-RAY PHOTOGRAPHS OF CASE 2.

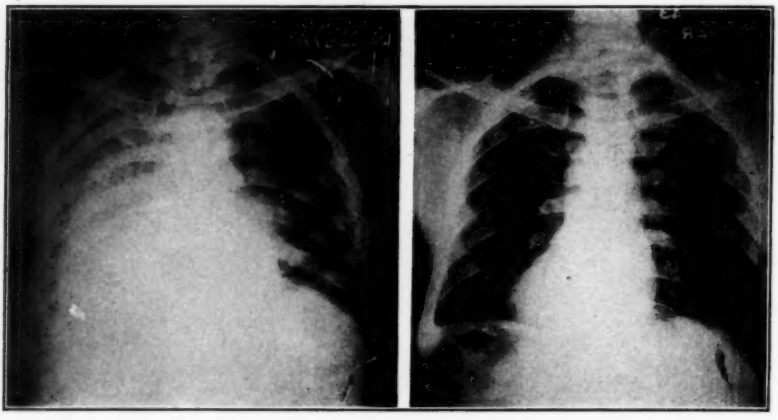


Fig. 3 Before penicillin therapy. Fig. 4 Four months after leaving hospital.

4th, and 7th day after the initial instillation. Five samples of exudate were taken from the area subjected to repeated treatments between the 1st and 15th day after beginning injections and, in each instance, cultures were sterile.

In spite of the disappearance of pneumococci from the site of infection receiving the repeated injections, the patient continued to be acutely ill. By additional explorations, a second pocket of empyema was found, the exudate from which contained Type VIII pneumococci. Before penicillin therapy was instituted into the second area, the patient began to cough up large quantities of purulent material. The course was interpreted as indicating that the second pocket was being drained through a bronchopleural opening. After 2 weeks the sputum became scanty and ceased to be purulent. The patient was improved but not afebrile.

Subsequently his temperature rose to 104.5°. A third pocketed area was discovered distant from the other two. No viable pneumococci were recovered from the purulent fluid of this area but a precipitin test performed by mixing the specimen of exudate with Type VIII antipneumococcus serum was strongly positive.

Into the third area 20,000 units of penicillin were injected. Within 48 hours the patient's temperature was normal and his convalescence

to recovery was rapid. X-ray photographs are appended. The last picture was taken four months after discharge from hospital.

Total Number of Intrapleural Injections of Penicillin: Four into the first focus, one into the third focus.

Amount per Dose: 20,000–15,000–20,000–25,000 units into the first pocket; 20,000 units into the third pocket.

Total Amount: 100,000 units.

Result: Pleural exudate of first pocket sterile 24 hours after first treatment. No recurrence of infection in first area but additional pockets were present. Final recovery was complete with limited residual pleural thickening.

Duration of Hospitalization: 62 days after beginning treatment, 15 days after treatment of last localized area of infection.

Case 3. Patient M.B., white, male, age 33 years.

Diagnosis: Lobar Pneumonia, Empyema. Pneumococcus, Type V.

The patient was treated for the first five days with sulfadiazine by mouth. Empyema was detected on 2nd hospital day. Local penicillin therapy was instituted on the 3rd hospital day by injecting 40,000 units intrapleurally. No additional treatments were given.

The pleural exudate obtained from each of two pre-treatment taps contained Type V pneumococci. From five subsequent aspirations performed two, six, eight and fifteen days after instillation of penicillin, 200-300 cc. of cloudy material were obtained. No pneumococci were present.

His general condition progressed satisfactorily except for low grade fever which continued for 16 days, together with a moderate leukocytosis, and some night sweats. It is interesting to note that in spite of the inability to demonstrate bacteriologically active infection, the exudate in the pleural cavity continued to accumulate for approximately two weeks before finally disappearing.

Resume: Total number of Intrapleural Injections of Penicillin: One.

Total Amount: 40,000 units.

Result: Pleural exudate sterile 48 hours after local treatment. No relapses. Clinically recovery was complete, but patient was not under observation for a sufficient length of time to observe the final degree of clearing of x-ray shadow.

Duration of Hospitalization after Beginning Treatment: 25 days.

TABLE IV

IRRITATING EFFECT OF PENICILLIN INJECTED INTRAPLEURALLY

Case No.	Diagnosis	Pleural Fluid W. B. C.	Penicillin Units	1st Day			2nd Day			4th Day		6th Day	
				Cells	Fever	Pain	Cells	Fever	Pain	Cells	Fever	Cells	Fever
1	TBC	590	40,000	Not done			1820			560			
2	Cardiac	255	12,500	64,200	+	+	36,800	+	—	3200	—	310	—
3	Cardiac	320	10,000	17,500	+	+	13,500	+	—	2920	—	810	—
4	Cardiac	620	10,000	14,500	+	+	8900	—	—	2750	—	1680	—
5	Cardiac	180	5,000	15,500	+	+	2190	—	—		—	1000	—
6	Pneu.	210	5,000	2975	+	+			—	1225	+		
7	Alc. Cirv.	770	5,000		—	—	1150	—	—			250	—
8	Cardiac	1830	5,000	5,500	—	—							
9	Cardiac Same as 2	340	Control	520	—	—		—		540	—		

The special features of the cases so far described consisted of: 1. The rapidity of sterilization of the empyemal cavity following injection of penicillin; 2. The persistence or probable reaccumulation of purulent exudate without demonstrable pneumococci; 3. The somewhat prolonged convalescence with low grade fever; 4. The ultimate recovery.

In considering an explanation of the course, which was characterized in each of the patients by rapid bacteriological "cure" but somewhat delayed clinical resolution, the possibilities which suggested themselves were that a small focus of undetected living organisms remained under the fibrin coating of the pleura even though aspirated material was sterile, or that the decomposition of the sterile pus produced toxic substances acting as irritants, or that the penicillin was itself irritating locally.

The latter possibility lent itself readily to testing. Accordingly, solutions containing from 5,000 to 40,000 units were injected intrapleurally into eight patients who suffered from hydrothorax due to various causes. The penicillin was introduced after removal of most of the transudate. Subsequent samples of the effusion were obtained on each of the following four to six days and the number of cells per cmm. was determined. The presence or absence of fever or thoracic pain was also noted. The results are contained in Table IV.

In each instance there was a definite but variable rise in the number of cells which was greatest the day after injection and gradually decreased during the ensuing days until a number slightly above the preinjection level was reached on the 4th to 6th day. Slight fever (100-101°) and some thoracic pain were present on the day following injection but disappeared within 48 hours.

In view of the evidence of a moderate irritating action of penicillin on the pleural surfaces, the next two patients received smaller doses of penicillin than those employed in the cases already described. The attempt was made to employ a sufficient number of units to obtain the necessary antibacterial effect but to minimize the untoward local reaction. That the dosage employed for that purpose was insufficient is evident from the relapses which occurred in the next two patients.

Case 4. Patient M.L., white, female, age 42 years.

Diagnosis: Lobar pneumonia, Bacteriemia, Empyema. Pneumococcus, Type V.

X-RAY PHOTOGRAPHS OF CASE 4.

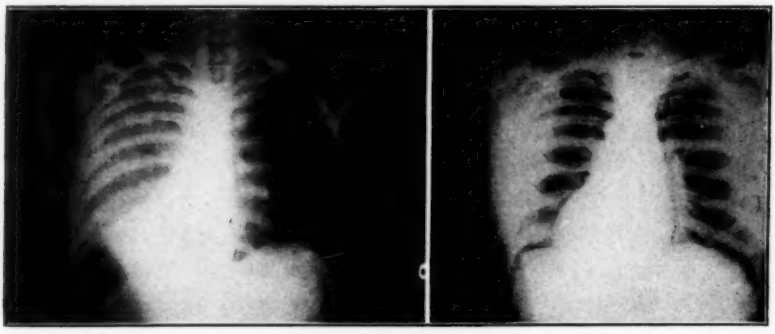


Fig. 5 Before penicillin therapy.

Fig. 6 Two months after leaving hospital.

On admission, treatment for the first three days consisted of penicillin given intravenously. A total of 130,000 units was administered. The bacteriemia cleared within 24 hours. Empyema was demonstrated on the 4th hospital day.

It is interesting to note that penicillin given during the early acute phase of the illness did not in this instance prevent the development of empyema.

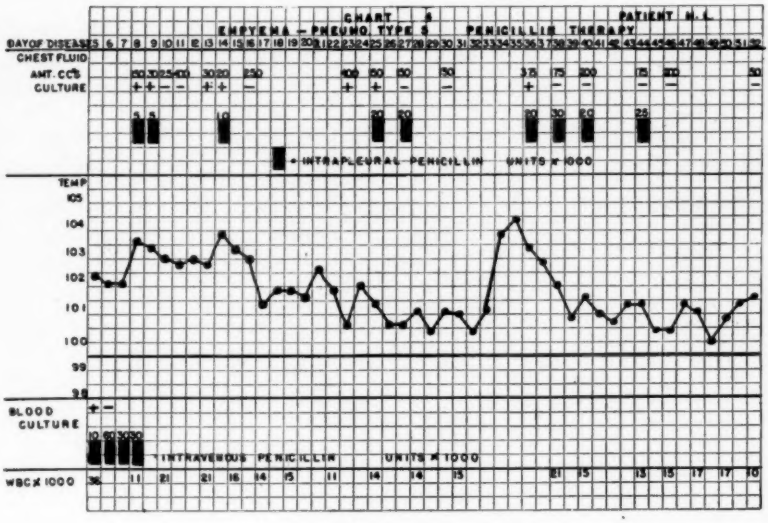
The difficulties in the course of the empyema in Case 4 which were referable to insufficient treatment are illustrated in Chart 4.

From Chart 4 it may be noted that following the injection of 5,000 units, the cavity was not sterilized but that after the second injection of an additional 5,000 units, two aspirations performed 24 and 48 hours later yielded material from which pneumococci were not obtained.

The patient, however, had three subsequent relapses as measured by a return of cultivable pneumococci to the pleural exudate. At each recurrence the dosage of penicillin was gradually increased. The infection was finally overcome by administering four separate doses on alternate days of 20,000-30,000 units.

In spite of her prolonged and irregular course due to inadequate treatment at the beginning, recovery occurred without any greater residue of pleural thickening than that seen in the other cases.

X-ray photographs are appended the last of which was taken two months after discharge from the hospital.



Resume: Total Number of Intrapleural Injections of Penicillin: 9.

Amount per Dose: As indicated in Chart 4 they varied from 5,000 to 30,000 units.

Total Amount: 155,000 units.

Result: Three recurrences of demonstrably viable pneumococci after transient periods of negative cultures. Ultimate recovery was complete with limited pleural thickening.

Duration of Hospitalization after Beginning Treatment: 79 days.

Case 5. Patient M.J., white, male, age 2 years, 3 months, admitted to Pediatric Service of Bellevue Hospital* on 6th day of disease.

Diagnosis: Lobar Pneumonia, Empyema. Pneumococcus, Type XVI.

The patient was treated with sulfathiazole and sulfadiazine for the first 12 days of hospitalization without notable improvement. The first successful thoracentesis yielding pus was performed in the 14th hospital day.

The treatment with penicillin in this patient was started by using small doses as in Case 4. The first injection consisted of 5,000 units.

* The patient's record is presented with the permission of Dr. James Wilson, Director of the Pediatric Service.

X-RAY PHOTOGRAPHS OF CASE 6.

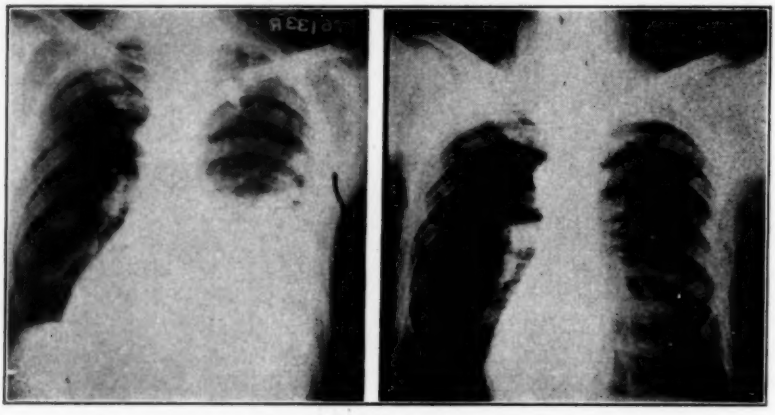


Fig. 7 Before penicillin therapy. Fig. 8 Four months after leaving hospital.

Two aspirations done one and five days after treatment yielded exudates which were sterile on culture. Viable organisms returned, however, within six days. Additional intrapleural doses of 15,000 and 10,000 units were administered which afforded only transient suppression of cultivable organisms.

Following the second relapse surgical drainage was carried out by rib resection. The patient recovered after a prolonged postoperative convalescence.

Resume: Total Number of Intrapleural Injections of Penicillin: 3.
Amount per Dose: 5,000—10,000—15,000 units.
Total Amount: 30,000 units.
Result: Penicillin therapy unsatisfactory due to insufficient dosage. Surgical drainage required. Recovery was complete.
Duration of Hospitalization: 131 days following thoracotomy.

Case 6. Patient, J.D., white, male, age 58 years.

Diagnosis: Lobar Pneumonia, Empyema, Pneumococcus, Type I.

The patient was treated with sulfadiazine by mouth for the first eight days of his illness. Empyema was diagnosed on the sixth hospital day. The empyemal strain was found to possess a definite degree of sulfonamide resistance. Following aspiration of the chest on the eighth

hospital day, 25,000 units of penicillin were instilled into the empyemal pocket.

Both of the pre-treatment specimens of pleural exudate were positive on culture for Type I pneumococci. Material aspirated on the day following treatment was sterile. Cultures of all subsequent samples were also negative.

The total amount of treatment given to the patient consisted of three injections of 25,000 units each injected on alternate days.

His clinical course, similar to that of the other patients who did not suffer relapse, was characterized by gradual improvement, but he maintained a slight fever of 99.5 to 100.5° until the 47th hospital day. The delayed absorption of the thick though sterile exudate was particularly striking.

In considering the possibility that the protracted low grade illness might be caused by active undetected infection, intensive therapy was carried out for six days. During the first three days 140,000 units of penicillin were given intravenously and 30,000 units were injected on two occasions intrapleurally. During the remaining three days 20 gms. of sulfadiazine were administered by mouth. No appreciable response occurred.

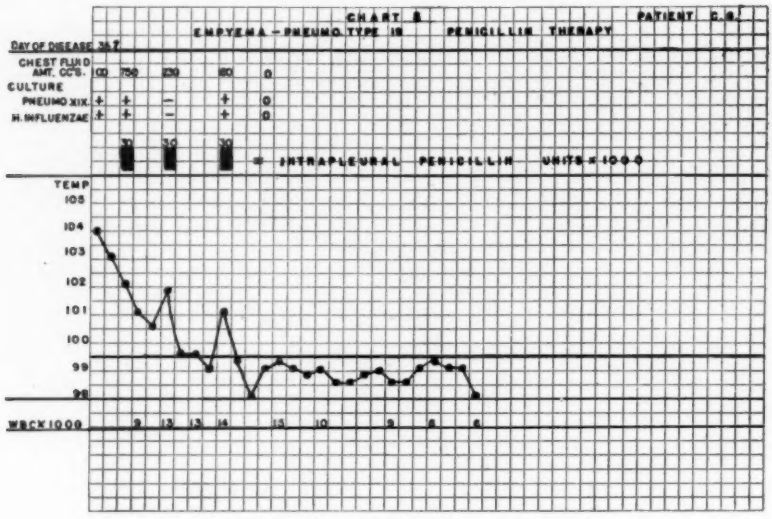
As an additional measure, when no signs of gradual absorption of the residual exudate could be detected, the site of the pleural pocket was irrigated with physiological salt solution in order to remove as much as possible of the degenerated abacterial pus. Following three irrigations on alternate days the presence of exudate was no longer demonstrable. No effusion reformed and progress to recovery was uneventful.

Resume: Total Number of Intrapleural Injections of Penicillin: 3.
Amount per Dose: 25,000 units.
Total Amount: 75,000 units.

(The amounts given above do not include the late period of additional therapy since the latter treatment did not influence the abacterial pus.)

Result: Pleural exudate sterile 24 hours after first treatment. No relapses. Recovery was complete with residual thickening of pleura.

Duration of Hospitalization after Beginning Treatment: 51 days.



Case 7. Patient C.G., white, female, age 27 years.

Diagnosis: Pneumonia, Pneumopyothorax. Pneumococcus, Type XIX, Hemophilus Influenzae.

The patient had been ill six weeks before admission with a disease which began as an upper respiratory infection. Her local physician had tapped her chest on one occasion and obtained fluid. When her condition remained unchanged she was admitted to the hospital suspected of having tuberculosis. Her course is illustrated in Chart 5.

On admission x-ray examination revealed the presence of both an effusion and air in the right pleural cavity; 100 cc. of thick purulent exudate were removed by thoracentesis. Pneumococcus, Type XIX and Hemophilus influenzae were both seen and cultured from the pus.

Following a second aspiration performed two days later, 30,000 units of penicillin were introduced after removal of 750 cc. of infected exudate.

Cultures of material obtained three days later yielded no growth. The suppression of H. influenzae is of interest since Fleming[4] did not find the strains of H. influenzae which he tested to be susceptible to the antibacterial action of penicillin. It seems likely that the concentration of penicillin introduced into the pleural cavity may have accounted for

X-RAY PHOTOGRAPHS OF CASE 7.

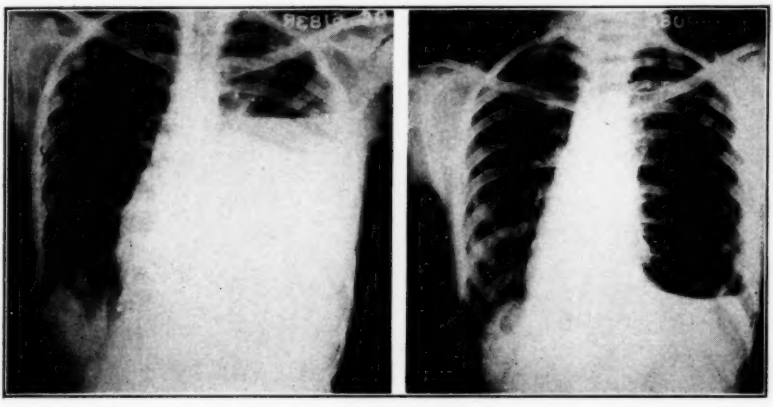


Fig. 9 Before penicillin therapy. Fig. 10 Two months after leaving hospital.

the effect or that the patient's strain was unusually susceptible to penicillin.

Four days after the second intrapleural treatment, pneumococci and H. influenzae were again seen in smears and cultivated from an aspirated sample of exudate. However, after the third instillation of 30,000 units subsequent efforts to obtain fluid were unsuccessful. The patient rapidly improved, her temperature becoming normal 18 days after beginning treatment.

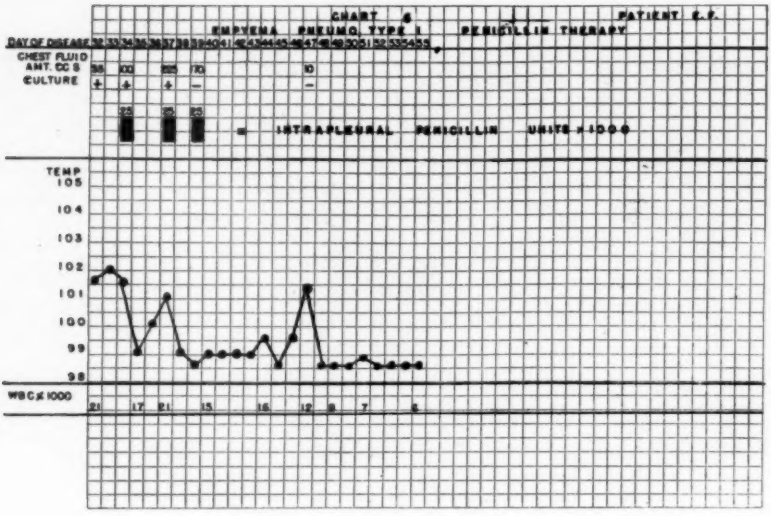
The unusual feature of the course of this patient was the persistence and even increase in the pneumothorax in spite of the rapid disappearance of the pyothorax. Her general clinical improvement paralleled her temperature course as presented in Chart 5. Up to the present time, four months after discharge from the hospital, no signs of effusion have developed in the affected side, but the bronchopleural fistula remains unhealed.

Resume: Total Number of Intrapleural Injections of Penicillin: 3

Amount per Dose: 30,000 units.

Total Amount: 90,000 units.

Result: One bacteriological relapse following second treatment. The pyothorax together with clinical and laboratory signs of infection disappeared but pneumothorax persisted.



Duration of Hospitalization Following Beginning of Treatment: 26 days.

Case 8. Patient E.F.,* colored, female, age 11 years.

Diagnosis: Lobar Pneumonia, Empyema. Pneumococcus, Type I.

The patient, treated on the Pediatric Service, received sulfadiazine for the first few days but continued to be ill. Suggestive signs of pleural effusion developed but pus was not obtained until 25 days after admission. Type I pneumococci were present in the exudate.

The course of the illness is represented in Chart 6.

The patient received 25,000 units of penicillin on three occasions, spaced three and two days apart respectively. Cultures of the exudate were sterile after the second treatment. The clinical improvement was rapid, her temperature becoming normal five days after receiving the initial injection of penicillin.

Resume: Number of Intrapleural Injections of Penicillin: 3.

Amount per Dose: 25,000 units.

Total Amount: 75,000 units.

Result: Pleural exudate sterile five days after beginning treatment. No relapses.

* See Page 156.

X-RAY PHOTOGRAPHS OF CASE 8.

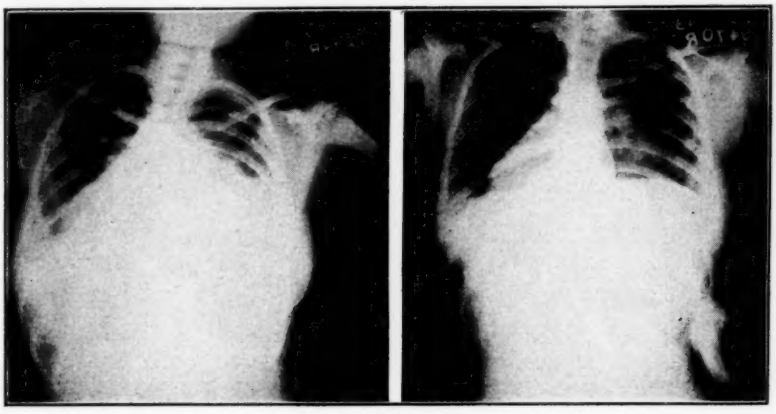


Fig. 11 Before penicillin therapy. Fig. 12 One week after leaving hospital.

Recovery was complete.

Duration of Hospitalization After Beginning Treatment: 21 days.

Discussion and Outline of Treatment

It is evident from the results which have been described that penicillin injected locally into the pleural cavity is capable under proper circumstances of effecting a cure in pneumococcal empyema without requiring surgical drainage. In developing the most suitable procedure for administering the drug consideration has been given to the therapeutic requirements with respect to amount of penicillin per dose, the frequency with which the injections should be repeated, and the number of repetitions that may be necessary. Although no arbitrary standards may be set at the present time, the favorable results so far obtained constitute a basis for formulating the details of treatment.

Amount of Penicillin, per dose, for Intrapleural Injection. In the two cases which received 5,000 to 10,000 units, pneumococci disappeared temporarily from the pleural exudate as determined by microscopic examination and culture of the specimens but relapses occurred in both instances.

When larger doses ranging from 25,000 to 40,000 units were employed, in only one instance did a relapse occur (Case 7), and even in

that case the infection was subsequently eliminated following one additional dose.

On the basis of present experience, therefore, 30,000 to 40,000 units appears to be an adequate amount per dose.

Frequency of Injections. The preliminary studies mentioned earlier in this article indicated that the activity of penicillin is retained for at least 48 hours to 72 hours after injection into an empyemal pocket. The fibrinous exudate appears to retard absorption but does not destroy the antibacterial quality at a rapid rate.

Furthermore, the tests carried out with repeated samples of exudate have shown that the initial suppression of the organisms that follows treatment is maintained for at least two to three days.

On the basis of these findings, therefore, no demonstrable advantage seems to be gained by performing thoracentesis oftener than every other day.

Number of Repeated Injections. Even though Case 2 recovered following a single injection of 40,000 units, and Case 1 received only two injections of 40,000 units each, treatment in the other patients was extended to at least three separate injections. In view of the fact that the end point of active infection is liable to be obscured by the persistence of low grade fever and the delayed absorption of the exudate even though sterile, the determination of the time at which treatment may be stopped has not been clearly defined. On the basis of practical experience, however, when clinical improvement appears to be progressive and the exudate remains sterile, three separate injections may, in most instances, be sufficient.

Plan of Treatment

Thirty to forty thousand units of penicillin contained in 30 to 50 cc. of isotonic salt solution injected intrapleurally on alternate days for at least three doses.

As a further measure in hastening recovery it is desirable at the time of bedside aspiration to irrigate the cavity with a few hundred cc. of physiological salt solution before introducing the penicillin and to repeat the procedure, if necessary, at intervals of several days after treatment is stopped in order to hasten the removal of the degenerated sterile exudate and minimize the reaccumulation of an effusion.

SUMMARY

I. *Lobar Pneumonia.* Penicillin has been found to be highly effective in the treatment of pneumococcal pneumonia.

Of 46 treated patients, 3 (6.5 per cent) died and 39 recovered in a striking manner indicating the special value of the drug. The response was not clearly defined in 4 patients, one of whom probably had primary atypical pneumonia and the other 3 had unrelated underlying pulmonary diseases which prolonged their illness beyond the usual course of pneumonic resolution.

Bacteriemia, which occurred in 14 of the patients, disappeared in every instance following injections of penicillin.

On the basis of quantitative data presented and discussed in this article, a tentative regime for the treatment of pneumonia with penicillin is outlined.

Factors relating to the relative values of penicillin and sulfadiazine in the treatment of pneumonia are discussed.

II. *Pneumococcal Empyema.* Eight patients with pneumococcal empyema have been treated by intrapleural injections of penicillin.

In seven, the infection was eliminated by the local therapy without requiring surgical drainage. Six of them recovered completely with only a restricted area of pleural thickening remaining as a permanent alteration.

In one patient, who had pyopneumothorax on admission, the pyothorax cleared up satisfactorily but the pneumothorax arising from a bronchopleural fistula which was present before treatment was begun, has persisted.

In another patient, who was insufficiently treated at the beginning with penicillin, relapse occurred and surgical drainage was instituted.

Following discharge from the hospital, the patients have returned for reëxamination at varying periods, after one week for one patient, and from 4 to 6 months for the others. With the exception of the case with pneumothorax, the others have remained well and free of symptoms.

Strains of pneumococci derived from the empyemal pus of patients whose pneumonia had been previously treated with sulfadiazine were found to possess varying but definite degrees of sulfonamide-resistance.

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A CRITICAL REVIEW OF GASTROSCOPY*

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IT IS now over ten years since gastroscopy by means of a flexible gastroscope was first introduced in this country at the Massachusetts General Hospital.[1] It, therefore, seems appropriate to make a decennial report on the present status of gastroscopy. During this period we have made 1600 gastroscopic examinations, or an average of only about three per week. I believe this indicates that the hospital staff is still not fully aware of the value of the procedure, nor the ease with which it can be performed. This is unfortunate, but must be expected with any new method of examination. On the other hand, the relatively small number of cases examined shows that we are not making it a routine method of study, and I believe this is fortunate since special studies should be undertaken for specific indications.

INSTRUMENT

In 1932 Rudolf Schindler, a German physician, collaborated with George Wolf, an optical physicist, to produce the Wolf-Schindler flexible gastroscope.[2] There are fifty-one elements in the optical system. Each lens is of short focal length and conveys the image to the next lens, so even when the flexible portion is curved it is still possible to see through it. The great flexibility of the lower part facilitates, as well as safeguards its passage through the esophagus into the stomach. The history of gastroscopy prior to 1932 deals with rigid instruments of various shapes and sizes, all of which were finally discarded as being too unsafe for practical use. The safety of the present instrument is attested by the fact that only one death occurred in over 22,000 examinations by sixty gastroscopists (0.004 per cent). Two modifications of the flexible gastroscope (Fig. 1) are worthy of mention: (1) The omniangle feature developed by Cameron which enables the operator to increase the range

* Presented at the Sixteenth Graduate Fortnight of The New York Academy of Medicine, October 12, 1943.

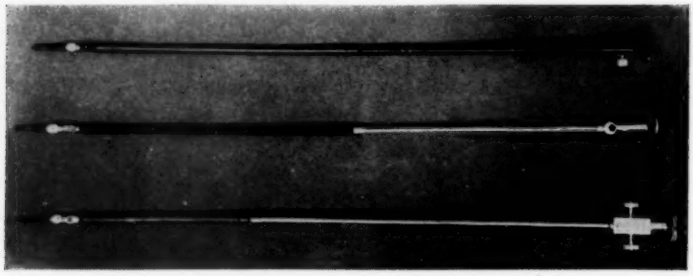

Fig. 1. Wolf-Schindler flexible gastroscope; Cameron omniangle flexible gastroscope showing mirror at distal end, angle of which is controlled by electromagnet; Taylor flexible gastroscope showing ratchet handle for controlling the flexible portion.

of vision by changing the angle of the mirror at the distal end. This is accomplished by an electromagnet controlled by a switch at the proximal end. Although this makes the instrument slightly more difficult to pass, I believe the better view obtained more than justifies its use. (2) The Taylor gastroscope,[3] the flexible part of which can be curled up or allowed to lie flaccid. It is flexible in all directions, but can be bent forward and backward in the plane of the objective up to the limits of optical flexibility. This control is obtained by a mechanical device manipulated from the proximal end of the instrument. By reason of this controllable flexibility, Taylor claims the following advantages: "Greater safety of instrumentation, less likelihood of failure of instrumentation, abolition of blind areas in the stomach, ability to move the instrument about in the stomach so as to inspect any particular area closely at will and from more than one angle and greatly increased illumination with less distortion of the image." On the other hand, Schindler believes that since the Taylor gastroscope has a shorter flexible portion and a longer rigid portion it will be less safe than the Schindler gastroscope because the rigid portion will extend below the cardiac orifice where trauma is likely to occur.

Technique

In spite of the fact that in many patients gastroscopy can be satisfactorily performed without preliminary sedation, I believe that medication with nembutal, morphine and atropine tends to allay apprehen-

sion and to provide better relaxation. The most satisfactory anesthesia of the throat is a simple gargle with 4 per cent cocaine or 5 per cent larocaine. The latter is unobtainable at the present time due to the war. Two per cent pontocaine gargle gives satisfactory anesthesia, but reactions have been reported.[4] Preliminary lavage or drainage of the stomach is necessary only when there is pyloric obstruction; since it takes extra time and is somewhat upsetting to the patient, it is to be avoided if possible. The use of small pillows instead of a head holder is to be recommended because it simplifies the technique, obviates the necessity for a trained assistant, and gives the patient more confidence in firm head support. My feeling is that in all matters of technique the simplest procedures compatible with good results are the best. Using this technique, more than one patient has voluntarily remarked that he would rather have the gastroscope passed than the nasal tube.

Indications and Contraindications

It is imperative for physicians to know when special procedures should be used. The indications for gastroscopy[5] may be listed as follows: gastritis; unexplained gastrointestinal hemorrhage; so-called "gastric neurosis"; unexplained persistent gastrointestinal symptoms, with negative or inconclusive x-ray examination; gastric ulcer, to determine the appearance and location of the lesion, to differentiate benign from malignant ulcer, and to follow the healing process in benign ulcer; duodenal ulcer, to study the gastric mucosa for the presence of gastritis, gastric erosions or gastric ulcerations; carcinoma, to determine the gross appearance, extent and operability of the lesion; polyposis; the so-called "postoperative stomach"; and occasional cases of suspected foreign body in the stomach. In addition to these indications, we have studied a number of other patients by gastroscopy, including those with pernicious anemia, food allergy, unexplained hematemesis or melena, hiatus hernia, deficiency disease, seasickness, lymphoma, sarcoma, benign tumor and submucosal tumor.

Although in many cases x-ray examination of the stomach may give a positive diagnosis, gastroscopy will often contribute additional information. No stomach which is producing symptoms should be considered normal without gastroscopic study. Gastroscopy bears much the same relationship to gastroenterology as cystoscopy bears to urology.

There are relatively few contraindications to the passage of the gas-

troscope. Esophageal obstruction is the only absolute contraindication. Aortic aneurysm probably should be considered a contraindication. In order to exclude esophageal obstruction it is the policy of the author always to have x-ray examination of the esophagus before gastroscopy. Among the relative contraindications which should be mentioned are esophageal varices, esophageal diverticulum, cardiac decompensation, cervical arthritis and marked debility. Extreme kyphosis or psychoneurosis also may be contraindications. Occasionally patients are so uncooperative that gastroscopy may be very difficult or unwise.

Gastritis

Gastritis is the commonest disease of the stomach. Everyone agrees that the best method of diagnosis is by gastroscopy. A positive x-ray diagnosis of gastritis when made by an observer experienced in the relief technique is usually of some significance, but should be checked by gastroscopy for the following reasons: (1) To determine whether or not gastritis is really present, for occasionally the enlarged rugae and other roentgen criteria in the diagnosis of gastritis seem to be of little or no significance; (2) to study the type, degree, location and extent of the gastritis if present; (3) to note the presence or absence of erosions or superficial ulcerations; (4) to demonstrate additional pathology, as, for example, a gastric ulcer not seen by x-ray; and (5) to help differentiate hypertrophic gastritis from carcinoma, sometimes an impossible differential diagnosis even with all methods of examination.

Acute or superficial gastritis is a disease usually of relatively short duration characterized by no typical symptomatology, but often accompanied by vague epigastric pain or distress, sometimes gas, nausea, vomiting and anorexia. Alcoholic gastritis is usually of the acute superficial variety, but Gray and Schindler[6] observed that the stomachs of 55 per cent of chronic alcoholics were essentially normal, the remaining 45 per cent showing mainly superficial gastritis, atrophic gastritis or a combination of the two. No method of diagnosis is reliable except gastroscopy. The gastroscopic picture is characterized by reddening of the mucosa, edema, and adherent secretion.

Chronic or hypertrophic gastritis often very closely simulates peptic ulcer in symptomatology. In a study of 117 cases of hypertrophic gastritis occurring without other gastric or duodenal pathology, Benedict[7] found the commonest symptom was epigastric pain, which occurred in

74 per cent of the cases. It was relieved by food or soda in 81 per cent, related to meals in 52 per cent and present at night in 21 per cent. Other frequent symptoms were vomiting (45 per cent), hemorrhage (42 per cent), gas (41 per cent), sour eructations (16 per cent) and heartburn (15 per cent). Clinical improvement was in most cases definitely correlated with the improvement in the gastric mucosa as seen by gastroscopy.

Atrophic gastritis, perhaps better called gastric atrophy, may occur as an independent disease characterized by vague indigestion, anorexia, weakness and anacidity, but the diagnosis is more commonly made when it occurs in association with pernicious anemia. In either case, the gastroscopic picture is unmistakable, the gastric mucosa exhibiting a smooth pale, grayish yellow or grayish green appearance with a network of blood vessels easily visible shining through the thin layers of the stomach wall. The probability that tumors of the stomach arise from an already diseased mucosa and the fact that they occur more commonly in an atrophic mucosa makes the diagnosis of gastric atrophy an important one from the standpoint of carcinoma.

Postoperative gastritis has been put in a class by itself by some observers, but I do not see how it can be so considered. Most stomachs that have been operated upon have been the site of ulcer or cancer and all ulcers and cancers are accompanied by some gastritis. The fact that a certain amount of gastritis persists after gastrojejunostomy or resection is to be expected. It is usually of the superficial or hypertrophic variety, or a combination of both.

Hemorrhage is a very important finding in gastritis and may occur in any type of gastritis with any degree of severity. In a study of 42 cases of bleeding from gastritis[8] I found 13 cases had bled from the superficial variety, 12 hypertrophic, 2 atrophic, 5 postoperative and 10 mixed. There had been 7 mild, 14 moderate, and 21 severe hemorrhages. X-ray examination was negative in 33 of the 42 cases. Erosions, superficial ulcerations and an edematous hyperemic friable mucosa with generalized oozing were the sources of the bleeding.

There is no specific treatment for superficial or hypertrophic gastritis. The superficial or acute variety usually responds fairly readily to the usual dietary measures with elimination of alcohol, limitation of tobacco, and dental attention. Sixty-three per cent of the cases of hypertrophic gastritis recently studied were relieved by bland diet with or

without alkali, belladonna, hydrochloric acid, etc. All cases of gastric atrophy respond to peroral or intramuscular liver therapy,[9] only a few respond poorly, the majority being entirely relieved. The gastroscopic appearance of the mucosa may be very much improved following adequate liver therapy.

The correlation of gastroscopic and pathological findings in gastritis[10] has been shown to be fairly accurate. Superficial gastritis as described by the gastroscopist corresponds to the acute exudative gastritis of the pathologist. The term atrophic gastritis is used by both gastroscopist and pathologist to denote the same type of mucosa. Hypertrophic gastritis as described gastroscopically corresponds to an exaggerated form of the physiological plasma cell and lymphocytic infiltration of the normal stomach. In the series of 51 cases of all types of gastritis carefully studied there was complete or partial gastroscopic-pathological agreement in 88 per cent.

Ulcer

In the study of gastric ulcer gastroscopy may reveal an ulcer not previously proven, may demonstrate multiple ulcers in a patient suspected of having only one lesion, may indicate that a severe gastritis accompanies the ulcer, and may be of assistance in differentiating a benign from a malignant lesion.

Walters and Clagett[11] have recently pointed out that although the accuracy of roentgenologic diagnosis of lesions of the stomach is remarkably high, there is always the chance that a small lesion or one situated high in the stomach may be overlooked. Gastroscopy should always be considered in a patient in whom there is a suggestion of a gastric lesion even though the roentgenologic examination does not reveal any abnormality. We know that erosions and superficial ulcerations frequently accompany gastritis and that such lesions are usually demonstrable only by gastroscopy. They indicate an inflammatory process with destruction of the mucosa and are, therefore, real ulcers even though there may be a difference of opinion as to whether or not they are true peptic ulcers. At any rate, there is no doubt that such erosions and superficial ulcerations may be the cause of symptoms and, therefore, the knowledge of their presence is of great importance. The fact that such lesions do not always cause symptoms is no reason to discredit their significance for a large peptic ulcer may be present without giving rise

to symptoms. The demonstration of more than one ulcer or of a severe gastritis accompanying an ulcer may alter the course of medical or surgical treatment, for a knowledge of the location and appearance of the ulcer or ulcers, and information as to the localization and severity of the gastritis will influence one's decision as to the medical regimen or the optimum time for surgery.

The differentiation of benign from malignant lesions of the stomach may be difficult or impossible. Templeton and Boyer[12] have pointed out, however, that inasmuch as no one method of examination is infallible, the use of all clinical, laboratory, roentgenologic and gastroscopic methods together is more likely to lead to a correct diagnosis. Each examination supplements the other and the wise physician will study the patient as a whole. When the roentgenologist is doubtful, the gastroscopist may be reasonably certain and vice versa. In a recent case the roentgenologist saw a lesion in the antrum, but was doubtful as to its nature. A gastroscopy was requested which showed a sloughing nodular ulcerating lesion obviously malignant (later proven at operation). In other cases the ulcer seen by gastroscopy may look benign, but x-ray may show so much rigidity that malignancy is almost a certainty. Usually an ulcer which appears to have sharp margins and a clean gray base is benign and an ulcer with slightly ragged, irregular or nodular margins and a dirty base is malignant. There will be a few cases, however, where all methods of study are doubtful, and unless complete healing takes place within three weeks they should be explored surgically. I believe that no patient should be discharged from the hospital with an unhealed gastric lesion.

Duodenal ulcer cannot be examined by gastroscopy, but the accompanying gastritis which pathologists say is always present can and often should be studied. Occasionally the gastritis is so severe that it is of more importance than the ulcer. I have seen a duodenal ulcer heal completely by x-ray, but symptoms persist or get worse due to severe gastritis. Hemorrhage supposed to have come from a proven duodenal ulcer may in fact have been coming partly or wholly from the gastritis. In a previous paper, 24 cases of gastritis and hemorrhage were discussed in which the question of ulcer was also raised. Since there was no evidence of an active ulcer crater by x-ray in 14 of those cases, the bleeding must have been from the gastritis. A knowledge of the appearance of the gastric mucosa may, therefore, be of importance in duodenal ulcer.

Gastrojejunal ulcer may occasionally be more readily demonstrated

by gastroscopy than by any other method of examination. As a rule, this is true only when the ulcer is on the gastric side of the stoma, for only a small part of the jejunum is visible by gastroscopy even under favorable conditions, and there are times when the stoma may not be seen at all. In doubtful cases gastroscopy should be performed.

Neoplasm

Carcinoma is the commonest neoplasm of the stomach and when it reaches a certain size the x-ray diagnosis is usually unmistakable. Unfortunately, by that time it may be inoperable. Even more unfortunate is the fact that before that time the patient may not have enough symptoms to consult a doctor, or if he does the doctor may not order an x-ray. Every patient over 35 with indigestion lasting more than a few days should have x-ray examination of his gastrointestinal tract. If such x-ray is negative or doubtful, he should have a gastroscopy. In the early diagnosis of carcinoma, gastroscopy will be of more value as it is used more frequently, but the average clinician accepts a negative x-ray as final and does not request gastroscopy. In the face of persistent symptoms, this is inexcusable, but is due in part to the relative novelty of the method and to the fact that many doctors and patients erroneously consider gastroscopic examination a terrific ordeal. In my experience roentgenologists are more apt to request gastroscopy than clinicians, and they do so whenever they are in doubt about the diagnosis, realizing the limitations of their own method and the supplemental value of gastroscopy. When x-ray examination is difficult due to obesity or high position of the stomach, gastroscopy may be easy and give a correct diagnosis at once. Helpful information as to the appearance, location, and extent of the growth may be added by gastroscopy.[13]

Since it is well known that an atrophic gastric mucosa provides a fertile soil for the development of carcinoma, the diagnosis of gastric atrophy, which can be made only by gastroscopy, assumes an added significance. Whenever this diagnosis is made, the patient should be followed by frequent x-ray and gastroscopic examinations to detect early malignancy. Gastric atrophy occurs not only in association with pernicious anemia, sprue, beriberi, pellagra and other deficiency diseases, but also as an independent entity. Vague indigestion and easy fatigability may point to gastric atrophy. According to Schindler,[14] superficial gastritis may go on to atrophy, which makes the diagnosis of gastritis and

especially the type of gastritis doubly important. In this connection also Hurst has remarked that carcinoma does not develop in a normal healthy gastric mucosa. We must, therefore, know more intimately by direct inspection the appearance of the gastric mucosa in many of our patients.

Other malignant tumors of the stomach are rare and can usually not be differentiated from carcinoma by any method of examination. Doubtful cases should be examined by gastroscopy.

In benign tumors of the stomach, gastroscopic examination is helpful in studying the base of the lesion for the extent of its attachment, and the surface of the lesion for the presence or absence of ulceration. Adenomatous polyps with a broad base tend to become malignant and should, therefore, be removed surgically. Some of the smaller polyps can be seen only by gastroscopy. The differential diagnosis between true polyp and pseudo-polyp can usually be made quite readily by direct inspection, for when the stomach is inflated with air the pseudo-polyps tend to disappear. Submucosal tumors may be observed directly as to size, presence or absence of ulceration, and normal or abnormal peristaltic wave. Two cases recently reported[15] come to mind, in one of which a diagnosis of cancer was changed by gastroscopy to leiomyoma or neurofibroma, later proven and successfully removed surgically; and in the other a stomach apparently normal by x-ray was shown to be the site of a submucosal antral tumor, later proven at operation to be an inoperable carcinoma of the pancreas invading the wall of the stomach.

Gastroscopy in the Armed Forces

In the present war the incidence of gastric disease is notably high. All methods of examining the stomach are, therefore, extremely important. When a soldier complains of digestive symptoms and x-ray study is negative, are we dealing with gastritis or malingering? When a sailor is constantly seasick, can he be used for occasional sea duty on large vessels, must he be kept for shore duty, or has he a really incapacitating gastritis? Gastroscopy is helping us to answer these questions.

Gastroscopy and X-Ray Examination

These two methods are so entirely different that comparison is not fair. One method supplements the other. X-ray examination should be done first because (1) it is easier, (2) in a given case it may furnish all the required information, and (3) it provides information as to the

normality of the esophagus which the gastroscopist should possess before blindly passing his instrument. In a general way it may be said that x-ray examination is of greater value in the study of gross changes, such as large ulcers and tumors, whereas gastroscopy is superior in the study of the finer mucosal changes as seen in gastritis. In modern medicine both methods are indispensable.

Conclusion

Gastroscopy with the flexible gastroscope is an easy and safe procedure, the value of which cannot be doubted. Attention has been called to the omniangle feature and controllable flexibility of certain instruments.

The simpler the technique the better. Four per cent cocaine gargle and small pillows for head support are to be preferred to more complicated methods.

The indications for gastroscopy have been outlined. No stomach which is producing symptoms should be considered normal without gastroscopic study.

The significance of hemorrhage from gastritis has been demonstrated by gastroscopy.

Gastroscopic and pathological findings in gastritis have been correlated.

The usefulness of gastroscopy in gastritis, ulcer and tumor has been critically reviewed.

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THE DIAGNOSIS AND TREATMENT OF PNEUMONIA*

THERE has recently been a large and increasing number of deaths from pneumonia in New York City in spite of the availability of the sulfonamide drugs. Because of this the Pneumonia Advisory Committee to the Department of Health has recommended the release of a statement to the medical profession calling attention to the necessity of early diagnosis and adequate treatment of pneumonia.

In New York City during the past month the number of deaths from primary pneumonia reported to the Department of Health has far exceeded the average number of deaths which would be expected during this period of the year. The number of reported deaths from primary pneumonia is larger than it has been for some years, and is particularly striking since it is occurring in an era when sulfonamide drugs are available. It is also high in comparison with deaths in pneumonia reported in many of the years of the pre-sulfonamide era. This increase was closely associated with the present outbreak of upper respiratory infections which may have contributed to the increase in the number of deaths.

The available evidence on cases of pneumonia in New York City during the present outbreak indicates that the etiology of such cases cannot be related to any particular microörganism and that many different microörganisms are involved. These include pneumococci of various types, the beta-hemolytic streptococcus, Staphylococcus aureus, influenza bacillus and Friedländer bacillus.

The intelligent management of the pneumonia patient requires that an etiological diagnosis be established. It has been disappointing to note that since the advent of the sulfonamides there has been a gradually decreasing interest on the part of physicians in determining the bacterial etiology of pneumonia in their patients. The number of bacteriological examinations of sputum performed by the Bureau of Laboratories of the New York City Department of Health has been

* The Pneumonia Technical Advisory Committee to the New York City Department of Health has recommended that this statement be brought to the attention of physicians of New York City.

insignificant in comparison with the number of reported deaths.

In considering the diagnosis and treatment of pneumonia patients, the following points are stressed:

1. There are a number of symptoms occurring in pneumonia which should lead to a suspicion of the presence of that disease and which often help in determining the occurrence of pneumonia in a patient suffering from upper respiratory infection or influenza. These include: (a) Shaking chill, (b) Pleural pain, (c) Rusty or bloody sputum, (d) Continued high fever, (e) Cyanosis, (f) Rising pulse rate, (g) Rising respiratory rate, (h) Shortness of breath, (i) Persistence of fever, accompanied by cough and expectoration, (j) Recurrence of fever following apparent recovery from the initial respiratory disease.

2. A knowledge of the bacterial etiology of the pneumonia is of great value in interpreting the course of the patient's disease, ascertaining reasons for failure of sulfonamide administration, indicating need for other types of therapy and interpreting the occurence of complications. It is desirable that a bacteriological examination of the sputum, including pneumococcus typings and blood cultures, be performed in all cases of pneumonia as soon as diagnosis is made. Such bacteriological examinations are an absolute necessity when patients do not respond favorably to 18 to 24 hours of adequate sulfonamide therapy. Delaying the bacteriological examination while awaiting results increases the difficulty of ascertaining the etiologic agent.

3. The sulfonamide drugs which are most effective in the treatment of bacterial pneumonia are sulfadiazine, sulfathiazole and sulfamerazine. An accepted dosage schedule for sulfadiazine and sulfathiazole consists of an initial dose by mouth of 4 grams followed by 1 gram every 4 hours until the symptoms have subsided and the temperature has been normal for 48 hours. In the case of sulfamerazine the schedule is similar except for a dosage of 1 gram every 6 to 8 hours instead of every 4 hours. Where patients are seriously ill or in the presence of vomiting, it may be desirable to substitute for the initial oral dose an intravenous dose consisting of 5 grams of the sodium salt of sulfadiazine or sulfathiazole or 4 grams of sodium sulfamerazine dissolved in a liter of physiological saline solution, or in a 5 per cent solution in sterile distilled water. Solutions of these drugs in physiological saline solution may be given subcutaneously in concentrations of 1 per cent or less. Sulfonamide administration should be accompanied by an

adequate fluid intake (3,000-4,000 ml. in an adult) and by the use of alkali sufficient to maintain an alkaline reaction of the urine (6 grams (90 grains) sodium bicarbonate as an initial dose and 2.5 grams (40 grains) of sodium bicarbonate every 4 hours has been recommended as the dosage for adults except when nephritis or other contraindicating disease is present). The primary purpose of such therapy is to maintain a urinary output of at least 1,200-1,500 ml. per day. Great caution must be exercised in the administration of fluids to patients with heart disease or to those who have evidence of congestive cardiac failure. The administration of fluid in these patients must be guided by the urinary output. Fluid administration in such patients should be limited to the minimum amount which will assure such urinary output.

The use of sulfonamide drugs in the treatment of simple upper respiratory infections is undesirable. When the severity of an upper respiratory infection is an indication for sulfonamide administration, investigation for the presence of pneumonia or other complicating disease should be instituted and the drug should be given in therapeutic amounts similar to the schedule indicated above. Small doses of sulfonamides over long intervals may produce drug-fast strains of microörganisms, and may sensitize the patient to the drug. Therefore, small doses of sulfonamides over long intervals are to be avoided.

Patients receiving sulfonamide drugs should be watched for the occurrence of symptoms due to the toxic action of the sulfonamides. These include: (a) Hematuria, oliguria, anuria and flank pain, (b) Skin rashes, (c) Drug fever, (d) Extreme nausea or vomiting, (e) Agranulocytosis.

With the exception of (a) these symptoms usually do not appear until the patient has been receiving the drug for about a week. If sensitivity to one drug becomes apparent, another should be substituted, although sulfamerazine and sulfadiazine should not be substituted for each other.

4. When a patient has been receiving adequate sulfonamide therapy in accordance with a schedule similar to that in (3) and does not respond to such medication within 18 to 24 hours, the patient should be re-evaluated. Such re-evaluation should include a complete physical examination to determine the status of the pneumonia, the presence of complications of the disease and of toxic reactions to sulfonamides; determination of the level of sulfonamide drugs in the blood and an evalu-

ation of the bacteriological findings in sputum and blood. If such re-evaluation indicates that the continued course of the patient's disease is due to pneumonia, and if the sulfonamide level in the blood is low, additional amounts of drug should be given. If the sulfonamide blood level is adequate (5-10 mg. per cent of free drug in the case of sulfadiazine and sulfamerazine and over 3 mg. per cent in the case of sulfathiazole) and if a type-specific pneumococcus (particularly of the common type) has been obtained from the sputum, or if a type-specific pneumococcus has been obtained from the blood culture, type-specific antipneumococcus serum therapy should be begun immediately. Such therapy should be preceded by the taking of a history of allergy and the performance of a skin and a conjunctival sensitivity test. At least 100,000-200,000 units of serum should be administered within 6 hours from the time when serum administration is begun.

5. The availability of specific therapy for pneumonia has not decreased the importance of careful repeated physical examinations of the patient and the many non-specific measures which assist the patient in combating his disease. These include *adequate nursing care*, provision of complete rest, oxygen therapy, maintenance of fluid balance, and the treatment of pleural pain with codeine. Such *treatment is best administered in a hospital*, particularly in the light of the present shortage of nurses. It is recommended that all cases of pneumonia be hospitalized early if hospital facilities are available. It is extremely important that all severe cases be hospitalized.

6. Patients who have had pneumonia for more than a few days and have not responded to adequate treatment should be suspected of having developed complications of the disease. The most important of these is empyema, the diagnosis of which is facilitated by an x-ray examination of the chest as is the spread of pneumonia to previously uninvolved portions of the lungs. Other complications include otitis media, thrombophlebitis, endocarditis and meningitis. The early diagnosis of empyema and its proper treatment may be life-saving.

PNEUMONIA TECHNICAL ADVISORY COMMITTEE TO THE DEPARTMENT OF HEALTH OF THE CITY OF NEW YORK

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PROCEEDINGS OF ACADEMY MEETINGS

STATED MEETINGS

JANUARY 6—*The New York Academy of Medicine.* Annual meeting, Scientific program with the Section of Surgery. ¶Executive session—a] Reading of the minutes; b] Presentation of Certificates of Fellowship. ¶Address of the President of the Academy, Arthur F. Chace. ¶Papers of the evening, Use of Plasma and Plasma Substitutes, Including the Treatment of Burns—a] Plasma and plasma substitutes, Robert F. Loeb, Lambert Professor of Medicine, College of Physicians and Surgeons, Columbia University; b] Treatment of burns, Allen O. Whipple, Professor of Surgery, College of Physicians and Surgeons, Columbia University. ¶Report on Election of Fellows.

JANUARY 20—*The Harvey Society in affiliation with The New York Academy of Medicine.* The Fourth Harvey Lecture, "The Anticoagulant from Spoiled Sweet Clover Hay," Karl Paul Link, Professor of Biochemistry, Wisconsin Agricultural Experiment Station.

SECTION MEETINGS

JANUARY 4—*Section of Dermatology and Syphilology.* Paper of the evening—Penicillin in the treatment of syphilis, John F. Mahoney, Senior Surgeon, U. S. Public Health Service; Director, Venereal Disease Research Laboratory, U. S. Marine Hospital. ¶Presentation of cases—a] From the Polyclinic Hospital; b] Miscellaneous cases. ¶General discussion. ¶Reading of the minutes. ¶Execuive session.

Section of Surgery—The Section joined with the Annual Meeting of the Academy on January 6, in presentation of its scientific program, and therefore held no meeting on its regular date in January.

JANUARY 11—*Combined Meeting of the New York Neurological Society and the Section of Neurology and Psychiatry.* Papers of the evening—a] Patients presenting neuro-ophthalmological conditions (Motion pictures), S. P. Goodhart, Montefiore Hospital; b] A case of postencephalitic cyclothymia, Foster Kennedy, Bellevue Hospital; c] A case of platybasia, B. C. Meyer, Mt. Sinai Hospital; d] A case of meningocele treated by destruction of the choroid plexuses (with lantern slides), Tracy J. Putnam, Neurological Institute; e] Demonstration of a defect in synthesis of acetylcholine in patients with myasthenia gravis, Clara Torda, Harold G. Wolff, New York Hospital. ¶Executive Session of the Section.

JANUARY 12—*Section of Historical and Cultural Medicine.* ¶Executive session—a] Reading of the minutes; b] Appointment of Nominating Committee. ¶Paper of the evening, The amenities of medical book collecting, Alfred Hellman. ¶Discussion opened by Eli Moschcowitz.

JANUARY 13—*Joint Scientific Session, Section of Pediatrics and Section of Otolaryngology.* Reading of the minutes. ¶ Papers of the evening—a] Differential diagnosis and treatment of sinusitis in children, D. E. Staunton Wishart, M. B., Surgeon-in-Chief, Department of Otolaryngology, Hospital for Sick Children, Toronto, Canada (by invitation); Discussion, J. Winston Fowlkes, Oscar M. Schloss; b] The use of sulfonamides in ear infections of children, John D. Kernan. Discussion, Murray H. Bass. ¶General discussion.

JANUARY 17—*Section of Ophthalmology.* Instruction Hour—Recent studies in color vision, Le Grand H. Hardy. ¶ Reading of the minutes. ¶ Case reports—a] Recurrence of fibrosarcoma of the orbit after seven years (results of radiotherapy), Abraham Kornzweig (by invitation); b] Eye muscle anomalies associ-

ated with aniseikonia—a preliminary report, Miss Edna Knauber (by invitation). ¶ Papers of the evening—a] Diagnosis of simple glaucoma in the preclinical stage by means of pupillography, Otto Lowenstein (by invitation), Mark J. Schoenberg; b] Practical surgical methods in glaucoma, Paul Chandler, Boston (by invitation); c] Diagnostic value of monocular occlusion, Kenneth Roper, Dartmouth Eye Institute (by invitation).

JANUARY 13—*Section of Genito-Urinary Surgery and the New York Urological Society.* Instead of the regular meeting for January 19, the Section held a scientific session with the New York Urological Society at the Yale Club. ¶ Paper of the evening, Studies in urinary calculosis, Linwood B. Keyser, Roanoke, Virginia. ¶ General discussion, Ephriam Schorr, Henry G. Bugbee, Nathaniel P. Rathbun, J. Sturdivant Read.

JANUARY 13—*Section of Otolaryngology.* The regular meeting of the Section was not held on January 19 because it met with the Section of Pediatrics in a joint meeting.

JANUARY 21—*Section of Orthopedic Surgery.* Because of the Annual Meeting of the American Academy of Orthopedic Surgeons in Chicago, no meeting was held of the Orthopedic Section of the Academy.

JANUARY 18—*Section of Medicine.* Reading of the minutes. ¶ Papers of the evening—a] Primary atypical pneumonia in private and general hospital practice, Major Norman Plummer, M.C., A.U.S.; Lt. Herbert K. Ensworth, M.C., A.U.S. (by invitation). Discussion, Russell L. Cecil; b] Clinical studies of immunity to influenza, Thomas Francis, Chairman of the Influenza Commission of the United States Army. Discussion, Colin M. MacLeod (by invitation). ¶ Executive session.

JANUARY 25—*Section of Obstetrics and Gynecology.* Executive session—Reading of minutes. ¶ Case Report—Extensive varix of vulva and vagina in full-term pregnancy. Delivery by cesarean section. (Lantern slides), Captain Samuel Adler. ¶ Papers of the evening—a] Preliminary report on use of vaginal smear in the diagnosis of malignancy (Lantern slides), Charlotte A. Jones (by invitation) Lieut. Commdr. Locke L. Mackenzie, Theodore Neustaedter; b] Dermatological lesions of the external genitals with special reference to lymphogranuloma (Lantern slides), Arthur W. Grace. ¶ General discussion.

AFFILIATED SOCIETIES

JANUARY 17—*New York Roentgen Society in affiliation with The New York Academy of Medicine.* Papers of the evening—a] The relationship of venography to venous thrombosis and pulmonary embolism, Harold Neuhof (by invitation), Ernest Sarason (by invitation). Discussion, David C. Bull (by invitation). b] Eosinophilic infiltration of the lungs, Herman Hennell (by invitation). Discussion, Joseph Harkay (by invitation); c] Thoracic manifestations of Boeck's sarcoid, Solon S. Bernstein (by invitation); Marcy L. Sussman. Discussion, Coleman B. Rabin (by invitation). ¶ General discussion. ¶ Executive session.

JANUARY 27—*New York Pathological Society in affiliation with The New York Academy of Medicine.* Papers of the evening—a] Autopsy observations in scleroderma, Margaret Bevans (by invitation); b] Homicide: Its problems for the medical examiner, Milton Helpern. ¶ Executive session.

DEATHS OF FELLOWS

BLODGETT, FRANK JEFFERSON: Sherman Square Hotel, New York City; born in Burlington, Vermont, October 15, 1857; died in New York City, October 30, 1943; received from the University of Vermont the degrees of Ph.B. in 1879 and M.A. in 1885; graduated in medicine from the University of Vermont in 1881; elected a Fellow of the Academy January 2, 1896; and served the Academy as a member of the Committee on Library, 1924-1926, and as its Chairman during 1926, and also as a member of the Council during 1926. He was a member of the State and County Medical Societies.

BULLOWA, JESSE GODFREY MORITZ: 62 West 87 Street, New York City; born in New York City, October 19, 1879; died in this city, November 9, 1943; received his B.A. degree from the College of the City of New York in 1899; graduated in medicine from the College of Physicians and Surgeons, Columbia University, in 1903; elected a Fellow of the Academy February 7, 1907.

Dr. Bullowa was clinical professor of medicine at New York University College of Medicine; visiting physician to the Harlem and Willard Parker Hospitals; consulting physician to the New York Infirmary for Women and Children and the Norwalk General Hospital, Norwalk, Connecticut; and consulting serologist to the Long Beach Hospital, Long Island. He was a diplomate of the American Board of Internal Medicine, a Fellow of the American Medical Association, and a member of the American Association of Immunologists, the Society for Experimental Biology and Medicine, and the State and County Medical Societies.

CARR, WALTER LESTER: 112 East 74 Street, New York City; and 66 Congress Street, Greenfield, Massachusetts; born in Lafayette, Jersey City, New Jersey, November 21, 1859; died in Greenfield, Massachusetts, February 2, 1944; graduated in medicine from the Medical Department of New York University in 1882; elected a Fellow of the Academy January 7, 1886; and served the Academy as a member of the Committee on Admissions from 1902 to 1907.

Dr. Carr was consulting pediatrician to the Letchworth Village, Thiells, New York Eye and Ear Infirmary, and Women's Hospital; director of pediatrics at the Midtown Hospital; emeritus clinical professor of pediatrics at New York University College of Medicine; a Fellow of the American Medical Association, a member of the American Pediatric Society, and a member of the State and County Medical Societies.

DOW, EDMUND LEROY: Watch Hill, Rhode Island, and Palm Beach, Florida; born in Baldwinsville, New York, in 1870; died in Palm Beach, Florida, December 1, 1943; graduated in medicine from the College of Physicians and Surgeons, Columbia University, in 1895; elected a Fellow of the Academy April 5, 1900.

Dr. Dow, who practiced medicine in New York for thirty years, retired in 1923. He was at one time a member of the American Association for the Advancement of Science, a member of the American Medical Association and the State and County Medical Societies.

FRISSELL, LEWIS FOX: 135 East 65 Street, New York City; born in Bloomfield, New Jersey, August 2, 1872; died in New York City, October 24, 1943; received from Yale University the degree of B.A. in 1895 and M.A. in 1897; graduated in medicine from the College of Physicians and Surgeons, Columbia University, in 1900; elected a Fellow of the Academy October 6, 1904; served the Academy as a member of the Committee on Library, 1914-1919; as Recording Secretary, 1937-1939; as Trustee, 1934-1936; and as a member of the Committee on Public Health Relations, 1915-1936.

Dr. Frissell was clinical professor of medicine at the College of Physicians and Surgeons, Columbia University, consultant in medicine to the St. Luke's Hospital, a

Fellow of the American College of Physicians and a member of the State and County Medical Societies.

GEIST, SAMUEL HERBERT: 100 East 74 Street, New York City; born in Brooklyn, New York, July 1, 1885; died in New York City, December 14, 1943; graduated in medicine from the College of Physicians and Surgeons, Columbia University, in 1908; elected a Fellow of the Academy March 5, 1914.

Dr. Geist was attending gynecologist to The Mount Sinai Hospital, clinical professor of gynecology at the College of Physicians and Surgeons, Columbia University, a diplomate of the American Board of Obstetrics and Gynecology, a Fellow of the American College of Surgeons, a Fellow of the American Medical Association, a member of the American Gynecological Society, and a member of the State and County Medical Societies.

KERRISON, PHILIP DAVID: 125 East 72 Street, New York City; born in Charleston, South Carolina, May 19, 1861; died in New York City, January 24, 1944; graduated in medicine from the Medical College of the State of South Carolina in 1895, and New York University College of Medicine in 1898; elected a Fellow of the Academy May 2, 1901.

Dr. Kerrison was consulting aural surgeon to the Manhattan Eye, Ear and Throat Hospital, and the Willard Parker Hospital; a diplomate of the American Board of Otolaryngology; a member of the American Otological Society, Inc., a member of the American Laryngological, Rhinological and Otological Society, and a Fellow of the American College of Surgeons.

KOPP, MARIE ELIZABETH: Ph.D.; 67 Echo Lane, Larchmont, New York; born in Lucerne, Switzerland, August 4, 1888; died in New York City, December 14, 1943; received the degree of Ph.D. from the University of Ferrara, Italy in 1912; elected an Associate Fellow of the Academy January 7, 1937.

LOWE, RUSSELL WALTER: 126 Main Street, Ridgefield, Connecticut; born in Oneida, New York, April 19, 1868; died in Ridgefield, January 3, 1944; graduated in medicine from the University of the City of New York Medical Department in 1888; elected a Fellow of the Academy March 1, 1894.

Dr. Lowe served as health officer from 1893 until 1939 and was town medical examiner in 1940. He was a Fellow of the American Medical Association and a member of the State and County Medical Societies.

MANGES, MORRIS: 1185 Park Avenue, New York City; born in New York City, May 10, 1865; died in this city January 26, 1944; graduated in medicine from the College of Physicians and Surgeons, Columbia University, in 1887; elected a Fellow of the Academy February 4, 1892.

Dr. Manges was consulting physician to the Mount Sinai Hospital, a member of the American Association for Thoracic Surgery, a Fellow of the American Medical Association, and a member of the State and County Medical Societies.

MAY, CHARLES HENRY: 70 East 66 Street, New York City; born in Baltimore, Maryland, August 7, 1861; died in New York City, December 7, 1943; graduated in medicine from the College of Physicians and Surgeons, Columbia University, in 1883; elected a Fellow of the Academy November 4, 1886.

Dr. May was consulting ophthalmic surgeon to the Bellevue, French, Mt. Sinai and Monmouth Memorial Hospitals; a diplomate of the American Board of Ophthalmology, a Fellow of the American Medical Association, a Fellow of the American College of Surgeons, and a member of the American Academy of Ophthalmology and Otolaryngology, the American Ophthalmological Society, the Association for Research in Ophthalmology, and the State and County Medical Societies.

NUTT, JOHN JOSEPH: 57 West 57 Street, New York City; born in Glencoe, Illinois, June 19, 1870; died in New York City, November 16, 1943; graduated in medicine from New York University College of Medicine in 1897 and Cornell University Medical College in 1899, elected a Fellow

of the Academy December 3, 1908.

Dr. Nutt was consulting orthopedic surgeon and professor of surgery to the New York Polyclinic Medical School and Hospital, consulting orthopedic surgeon to the Nyack Hospital, Long Beach Hospital and Rockland County and Suffern Hospitals, and orthopedic surgeon to the Willard Parker Hospital. He was a diplomate of the American Board of Orthopedic Surgery, a Fellow of the American College of Surgeons, a Fellow of the American Medical Association, and a member of the American Academy of Orthopedic Surgeons, the American Orthopaedic Association, and the State and County Medical Societies.

ROBINSON, HORACE EDDY: Pleasantvile, New York; born in Portland, Maine, January 16, 1887; died in Pleasantville, January 11, 1944; graduated in medicine from Tufts College Medical School, Boston, in 1912; elected a Fellow of the Academy October 7, 1920.

Dr. Robinson was chief of the division of contagious diseases at Grasslands Hospital, Elmsford; attending pediatrician to the Northern Westchester Hospital, Mount Kisco; a Fellow of the American Medical Association, and a member of the State and County Medical Societies.

ST. GEORGE, ARMIN VON: 773 Park Avenue, New York City; born in Jersey City, March 9, 1892; died in New York City, November 20, 1943; graduated in medicine from the College of Physicians and Surgeons, Columbia University, in 1914; elected a Fellow of the Academy May 4, 1933; and served the Academy as a member of the Committee on Medical Education from 1939 through 1941.

Dr. St. George was assistant director of the pathology laboratories of Bellevue Hospital, consulting pathologist to the Medical Center of Jersey City, visiting physician to the Lenox Hill Hospital, and associate professor of forensic medicine at New York University. He was a diplomate of the American Board of Pathology, a Fellow of the American Medical Association, and a member of the American Association of Pathologists and Bacteriologists, the American Society of Clinical Pathologists and the State and County Medical Societies.

STENSON, WALTER THOMAS: 45 East 85 Street, New York City; born in Sherbrooke, Ontario, Canada, November 6, 1895; died in Punta Gorda, Florida, December 8, 1943; graduated in medicine from McGill University in 1922; elected a Fellow of the Academy March 1, 1928.

Dr. Stenson was associate attending surgeon to the Lenox Hill Hospital, a Fellow of the American College of Surgeons, a Fellow of the American Medical Association, a diplomate of the American Board of Surgery, and a member of the State and County Medical Societies.

VOGT, ALFRED: Ramistrasse, 73, Zurich, Switzerland: born in Menziken (Aarau) Switzerland, October 31, 1879; died in Zurich, Switzerland, December 10, 1943; graduated in medicine from the University of Zurich; elected an Honorary Fellow of the Academy March 2, 1933.

Dr. Vogt was professor of ophthalmology at the University of Basle from 1918 to 1923 and professor of ophthalmology at the University of Zurich since 1923. He was author of numerous books and textbooks on ophthalmology.

WELT-KAKELS, SARA: 35 East 61 Street, New York City; born in Austria, December 12, 1860; died in New York City, December 26, 1943; graduated in medicine from the University of Zurich, Switzerland, in 1885; elected a Fellow of the Academy February 1, 1894.

Dr. Welt, who was adjunct pediatrician to the Mount Sinai Hospital, was the first woman pediatrician to serve at that institution, having joined that hospital in 1887. She was a member of the State and County Medical Societies and a Fellow of the American Medical Association.

LECTURES TO THE LAITY

Ninth Series

WAR AND THE EXPANDING FRONTIERS OF MEDICINE

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COLIN M. MACLEOD, M.D.

Professor of Bacteriology, New York University College of Medicine

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